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## ERRATA.

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| Page. | Line. | |
|---|---|---|
| 1864 | 23* | *For* " 8% sodium hydroxide solution " *read* " methyl alcohol." |
| ,, | 5* | *For* " $C_{17}H_{19}O_6N$ " *read* " $C_{17}H_{19}O_5N$." |
| 1980 | 9 | *For* " α-methylglucoside " *read* " β-methylglucoside." |

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| | | |
|---|---|---|
| 15 | | In formula (X) interchange the median CHMe and $CH_2$. |
| 74 | 30 | *For* " MacKenzie " *read* " McKenzie." |

* From bottom.

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THE CHEMICAL SOCIETY.

# 1. *Preparation of Phthalocyanine-like Pigments related to the Porphyrins.*

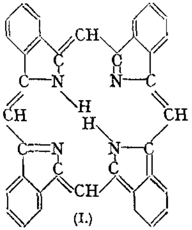
By Charles Enrique Dent.

*Methylenephthalimidine* has been prepared by crystallising phthalimideneacetic acid from water at 80°. It is a stable yellow crystalline compound which readily polymerises when heated. Phthalonitrile, a metal compound, and either methylenephthalimidine or phthalimideneacetic acid readily react together to give new pigments, of which the copper derivative has been identified as *copper tetrabenzotriazaporphin.* The new pigments are green to blue and resemble in properties the phthalocyanines, to which they are closely related.

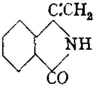
Benzylidenephthalimidine and ethylidenephthalimidine also have been prepared by new and improved methods.

It has been shown (Dent, Linstead, and Lowe, J., 1934, 1933) that there exists a close similarity in structure between the phthalocyanines and the porphyrins; it seemed reasonable to suppose, therefore, that the technique used for preparing phthalocyanines could be applied to the synthesis of substances of true porphyrin structure.

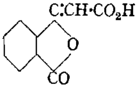
The object of this work was to prepare derivatives of tetrabenzoporphin (I), *i.e.*, phthalocyanine in which the four "linking" nitrogen atoms are replaced by methin groups. It was considered that compounds of this type would be most readily prepared



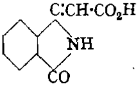

(I.)




(II.)




(III.)




(IV.)

from intermediates which are known to give phthalocyanines but in which one nitrogen atom is replaced by a methin group. *o*-Cyanophenylacetylene has already been examined, without result, by Linstead and Noble (J., 1937, 934) and, acetylenic compounds being perhaps unsuitable on account of their instability, attention was concentrated upon *o*-cyanoacetophenone and *methylenephthalimidine* (II). The present paper describes the preparation and properties of methylenephthalimidine and some closely related compounds.

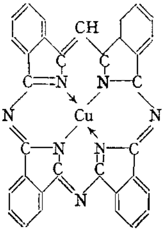
Phthalic anhydride was condensed with potassium acetate in the presence of acetic

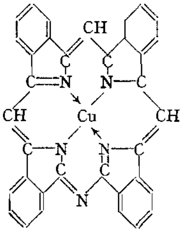
anhydride to give phthalideneacetic acid (III) (Gabriel and Neumann, *Ber.*, 1893, **26**, 951), which was converted, by solution in dilute aqueous ammonia and precipitation with hydrochloric acid (Gabriel, *Ber.*, 1877, **10**, 1556; Roser, *Ber.*, 1884, **17**, 2623), into phthalimideneacetic acid (IV). This acid lost carbon dioxide on crystallising from water at 70—90°, giving methylenephthalimidine. All these compounds polymerise readily at about 100°.

The action of methylmagnesium iodide upon phthalimide, of formaldehyde upon phthalimidine, and of ammonia upon methylenephthalide failed to give methylenephthalimidine.

Methylenephthalimidine, when heated with a metallic compound (cf. iminophthalimidine; Dent, Linstead, and Lowe, *loc. cit.*), alone or in presence of phosphoryl chloride, aluminium chloride, or chlorosulphonic acid in a suitable solvent, did not give a compound resembling a porphyrin or a phthalocyanine. When, however, a mixture of phthalonitrile, methylenephthalimidine or the more readily available phthalimideneacetic acid, and copper was heated, it readily gave a pigment greener than copper phthalocyanine, together with some resinous matter. This reaction was investigated further. The usual procedure was to mix equimolecular proportions of phthalonitrile and phthalimideneacetic acid with half the molecular proportion of the metal compound. In order to avoid undue polymerisation the mixture was either immersed in a bath at 250° or added direct to chloronaphthalene at 250°. The new coloured compound was formed in good yield in a few minutes. The product thus obtained by means of cupric or cuprous chloride was identified as *copper tetrabenzotriazaporphin* * (V). It is noteworthy that an unchlorinated compound is formed from cupric chloride. In the corresponding phthalocyanine reaction (Dent and Linstead, J., 1934, 1028) a monochlorinated phthalocyanine results.

(V.)




(IX.)

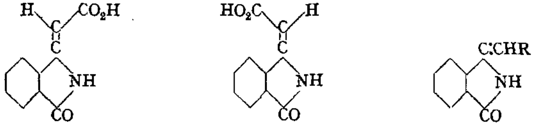
It seemed remarkable that methylenephthalimidine (or phthalimideneacetic acid) should react only in the presence of phthalonitrile and moreover that the combining proportions should be different from the proportions taken for reaction. The same product was obtained when the latter proportions were varied considerably. Although the analyses were conclusive, an independent check was considered advisable. Accordingly 4-chlorophthalonitrile was brought into reaction with an equimolecular proportion of phthalimideneacetic acid in the presence of cuprous chloride under the usual conditions. The purified *product* was greener than but otherwise similar in properties to the corresponding compound from phthalonitrile. It appeared to be homogeneous and contained exactly three chlorine atoms per molecule. This proves that there are three phthalonitrile units and one methylenephthalimidine unit in the pigment molecule.

*N*-Methylphthalimideneacetic acid (Gabriel, *Ber.*, 1885, **18**, 2451) did not react with phthalonitrile and cupric chloride, as would be expected owing to the absence of the imino-hydrogen atom.

The reaction of different metallic compounds with the mixture of phthalonitrile and phthalimideneacetic acid appears to be as general as the reaction with phthalonitrile alone. Other metallic derivatives have been obtained, all closely resembling the correspond-

* Nomenclature according to Helberger, *Annalen*, 1937, **529**, 205.

ing phthalocyanines in chemical and physical properties. They will be described in a later paper.




(VI.) (VII.) (VIII.)

There are two possible stereoisomeric forms of phthalimideneacetic acid (VI and VII). The presence of a hydrogen atom in the position *cis* to the imino-group is apparently necessary in order that the compound may enter into the porphyrin molecule, since the *trans*-atom is clearly the one which remains. It is believed that phthalimideneacetic acid has the structure shown in (VI) for the following reasons: complete decarboxylation always occurred; this would not be necessary in the case of (VII): protection of the carboxyl group by esterification or by conversion into its copper salt completely inhibited its reactivity in the presence of phthalonitrile.

Ethylidenephthalimidine (VIII, R = Me) has been prepared by an analogous method to the methylene compound starting from α-phthalidenepropionic acid and by treating ethylidenephthalide with ammonia. It appears to be identical with the compound prepared by Beis (*Compt. rend.*, 1904, **138**, 988; **139**, 62) by the action of ethylmagnesium bromide on phthalimide. It is a stable white crystalline compound not exhibiting the tendency towards polymerisation shown by the methylene compound. The reaction with phthalonitrile is being investigated.

Benzylidenephthalimidine (VIII, R = Ph) was prepared by passing ammonia into molten benzylidenephthalide. It is a yellow crystalline compound soluble in most organic solvents but most suitably crystallised from glacial acetic acid. Its chemical properties are under investigation.

Helberger (*Annalen*, 1937, **529**, 205) has described the preparation of porphyrin-like pigments by heating together *o*-chloroacetophenone and cuprous cyanide in quinoline. In this way he has prepared copper tetrabenzomonoazaporphin (IX), which he assumes is formed by the interaction of three molecules of nascent *o*-cyanoacetophenone with one molecule of phthalonitrile. The formation of the latter compound, seemingly by replacement of both the substituents of the *o*-chloroacetophenone, is remarkable and he suggests that the presence of phthalonitrile is necessary to start the reaction of the *o*-cyanoacetophenone. There is a fundamental similarity here with the behaviour of methylenephthalimidine. On the other hand, Helberger obtained products with three "linking" methin groups, whereas those described in this paper contain only one. It is difficult to agree, therefore, with Helberger that methylenephthalimidine is an intermediate in the formation of his products, though this could occur in the following stages:

The writer is indebted to Dr. R. P. Linstead for reminding him of the similarity between the last stage depicted above and the well-known molecular rearrangement of *o*-cyanobenzoic acid to phthalimide.

EXPERIMENTAL.

*Preparation of Phthalideneacetic Acid* (III) (modification of the method of Gabriel and Neumann, *loc. cit.*).—270 G. of phthalic anhydride were dissolved in 360 c.c. of acetic anhydride at 100°, 180 g. of fused potassium acetate added, and the temperature raised during 15 minutes to 150° and maintained, if necessary, for the completion of the reaction. The

mass thickened, then thinned, and finally set hard and showed a purple colour on the surface. At this stage it was withdrawn from the bath (to avoid polymerisation), cooled, added in small amounts to a large volume of water, washed with hot water and with alcohol, and dried at 60°. Yield, 140—160 g. of a pale brown solid insoluble in low-boiling organic liquids and completely soluble in dilute aqueous ammonia. Increasing the amount of potassium acetate to 270 g. gave a yield of 190 g. of good quality acid.

*Preparation of Phthalimideneacetic Acid* (IV) (after Gabriel and Roser, *locc. cit.*).—40 G. of phthalideneacetic acid were added to 40 c.c. of concentrated aqueous ammonia and 400 c.c. of water at 0—5°. After 30 minutes' stirring, the wine-red solution was filtered and made acid to Congo-paper by the gradual addition of dilute hydrochloric acid (1 : 1), the temperature being maintained at 0—5°. The precipitated phthalimideneacetic acid was collected after 30 minutes, washed with cold water, and dried at 40°. Yield, 38 g. of reddish crystalline acid containing two molecules of water of crystallisation. It could be purified by dissolving it in a slight excess of ammonia solution and precipitating it with a slight excess of hydrochloric acid (Found: C, 53·35; H, 4·4; N, 6·25. Calc. for $C_{10}H_7O_3N,2H_2O$: C, 53·3; H, 4·9; N, 6·2%). The author was unable to check Gabriel's observation that phthalimideneacetic acid could be purified by crystallisation from hot water, methylenephthalimidine being always obtained. The solution in water was acid to Congo-red, but became neutral on boiling. The dihydrate melted at 120° with instant effervescence; on further heating a resinous polymer was obtained.

*Preparation of Methylenephthalimidine.*—24 G. of phthalimideneacetic acid dihydrate, added to 600 c.c. of water at 80°, rapidly dissolved and effervesced vigorously. At the moment the gas evolution appeared to be nearly complete the solution was filtered through a preheated funnel into a flask immersed in ice, and cooled rapidly as possible by swirling. *Methylenephthalimidine* separated in golden-yellow crystals, which were collected after 30 minutes, washed with cold water, and dried at 40°. Yield, 11 g. The time of solution and decomposition at 80° was most critical and was usually about 30—60 seconds. It was difficult to obtain a product with the full carbon content, owing to the likelihood of contamination with undecarboxylated material. On the other hand, if the substance was maintained too long at 80°, a milkiness due to polymerisation soon developed; this always contaminated the product, since it passed through the filter paper in the first filtration (Found: C, 73·4, 73·3; H, 4·65, 4·7; N, 9·7; *M*, cryoscopic in phenol, 140±10. $C_9H_7ON$ requires C, 74·5; H, 4·8; N, 9·7%; *M*, 145).

Methylenephthalimidine melts when immersed in a bath at 120—125°. If slowly heated, it sinters at about 230° and melts at 250—260° owing to polymerisation. When heated to a higher temperature, it rapidly polymerises to a resinous substance, hard and brittle when cold and usually red. It is readily soluble in cold acetone, methanol, and other organic solvents, but much less so in warm water. When added to boiling water, it dissolves and then in a few seconds polymerises, forming a white milky colloidal solution which barely shows signs of settling after a week.

*Preparation of Copper Tetrabenzotriazaporphin* (V).—An intimate mixture of 5 g. of methylenephthalimidine (2 mols.) (or 7·75 g. of phthalimideneacetic acid), 4·4 g. of phthalonitrile (2 mols.), and 2·5 g. of cupric chloride dried at 100° (1 mol.), spread in a thin layer in a 250 c.c. beaker and immersed in an oil-bath at 250°, soon melted and in a few minutes the separation of a lustrous purple solid began. After 15 minutes' heating, the mass was cooled and ground and the black powder (9 g.) was extracted with hot alcohol until no more brown impurity was removed. The residue (3·9 g.) was purified by continuous extraction with chloronaphthalene. A yellow resinous impurity which sometimes still remained and could be seen by microscopic examination was most conveniently removed by refluxing with a solution of sodium amyloxide (1 g. of sodium in 50 c.c. of amyl alcohol), filtering, and washing. About 2 g. (30% yield) of *copper tetrabenzotriazaporphin* were obtained in needles of "bronzy" lustre very similar in appearance to copper phthalocyanine. When rubbed on paper the crystals gave a greenish-blue smear comparable with that of metal-free phthalocyanine. The substance was insoluble in low-boiling solvents, also in hot or cold pyridine (distinction from Helberger's copper tetrabenzo-mono- and -di-azaporphins) (Found: C, 68·9; H, 3·0; N, 16·9; Cu, 11·5. Found for a sample sublimed in a vacuum at 550°: C, 68·9; H, 2·6. $C_{33}H_{17}N_7Cu$ requires C, 68·9; H, 3·0; N, 17·0; Cu, 11·1%).

Copper tetrabenzotriazaporphin is greener than copper phthalocyanine but otherwise remarkably similar in its properties. It can be obtained in lustrous purple needles by continuous extraction with chloronaphthalene. It is readily soluble to a brown solution in concentrated sulphuric acid, from which it is thrown down as a green flocculent precipitate

on dilution into water. A smear of the compound on paper immediately turns purple when treated with nitrogen peroxide vapour, but regains its original colour in a few hours. The compound sublimes with a greenish-blue vapour at a dull red heat without much decomposition. A characteristic reaction occurs when a few drops of nitric acid are added to a olution of the compound in sulphuric acid : a brilliant red colour is produced, and a blood-red recipitate is obtained when the mixture is poured into water. The red compound is not table and becomes browner and weaker in shade after a few minutes.

*Varying proportions of reactants.* In the above preparation, equimolecular proportions of hthalimideneacetic acid and phthalonitrile were taken : under these conditions the formation f copper phthalocyanine or of copper tetrabenzodiazaporphin has never been observed. When 1 mol. of phthalimideneacetic acid was used with 3 mols. of phthalonitrile and 1 mol. f cuprous chloride, an excellent yield (70—80%) of pigment was obtained, contaminated, owever, with a small amount of copper phthalocyanine. When 3 mols. of phthalimideneacetic acid were treated with 1 mol. of phthalonitrile and 1 mol. of cuprous chloride, only a ellowish-brown insoluble compound was obtained.

*Reaction in the presence of a diluent.* A purer product was generally obtained when the eaction mixture was slowly added to 2½ times its weight of chloronaphthalene at 250°. Reaction was very rapid, frothing due to water evolution taking place in the early stages, and he mixture was usually stirred for 30 minutes at 250° before being cooled and worked up in he way already described. The reaction also took place in the presence of pyridine provided hat the concentration of the reactants was very high (about 50%).

*Sulphonation of Copper Tetrabenzotriazaporphin.*—The crude washed reaction product was lissolved in 5% oleum (20 parts) and heated at 100° until a sample diluted with water gave a lear green solution on addition of dilute aqueous ammonia (30—60 mins.). The acid mixture vas poured into an excess of cold water and the precipitated sulphonic acid was collected and vashed with a little cold water. It could be either dried as the sulphonic acid, or neutralised vith ammonia and the solution evaporated to give the ammonium salt. The sulphonic acid vas green and only slightly soluble in cold water. The ammonium salt was bluer than the cid and was readily soluble in water to a bluish-green solution.

*Preparation of Copper Trichlorotetrabenzotriazaporphin.*—A mixture of 13 g. of phthalmideneacetic acid (2 mols.), 9·5 g. of 4-chlorophthalonitrile (2 mols.), and 6 g. of cuprous hloride (1 mol.), added during 10 minutes to 100 c.c. of chloronaphthalene at 250° and nechanically stirred, soon developed a strong green colour and after 30 minutes became iscous. It was heated altogether for 1½ hours at 250° and cooled. The solid product, after eing collected and washed with benzene (yield, 12·0 g., dried at 90°), was green and gave the haracteristic red colour reaction with a mixture of sulphuric and nitric acids. A pure sample vas obtained, as described previously, by washing and extraction, in short thick microscopic eedles which gave a bluish-green smear when rubbed on paper [Found : Cl, 15·85; Cu, 9·15 *i.e.*, 3 atoms of Cl to 1 atom of Cu). *Copper trichlorotetrabenzotriazaporphin*, $C_{33}H_{14}N_7Cl_3Cu$, equires Cl, 15·7; Cu, 9·35%].

*Copper Phthalimideneacetate.*—To a neutral solution of ammonium phthalimideneacetate repared from 20 g. of the acid (2 mols.) in 200 c.c. of water, a solution of 11·1 g. of copper ulphate (1 mol.) in 100 c.c. of water was added. The dull greenish precipitate was collected, vashed with cold water, and dried (yield, 14·3 g.) [Found : Cu, 14·6. $(C_{10}H_6O_3N)_2Cu$ requires Cu, 14·6%]. *Copper phthalimideneacetate* gave only a trace of pigment when heated with hthalonitrile and copper bronze. When this experiment was repeated quantitatively on a arger scale with and without chloronaphthalene as diluent, only a 10% yield of copper etrabenzotriazaporphin was obtained (Found : C, 68·85; H, 2·85%).

*Methyl Phthalimideneacetate.*—The silver salt (10·2 g., prepared from the ammonium salt nd silver nitrate in neutral solution) was refluxed for 3 days with 9 c.c. of methyl iodide and 50 c.c. of dry ether. The sticky yellow residue remaining after filtration and evaporation of he solvent was crystallised several times from methanol, giving buff crystals of the ***methyl*** ***ester***, m. p. 125—127°, in poor yield (Found : C, 64·95; H, 4·3; N, 7·8. $C_{11}H_9O_3N$ requires C, 65·0; H, 4·4; N, 6·9%). The ester gave no trace of pigment when heated with hthalonitrile and cuprous or cupric chloride.

*Preparation of Ethylidenephthalimidine* (compare Gabriel and Michael, *Ber.*, 1878, **11**, 1013). —(a) 72·5 G. of phthalic anhydride (1 mol.) were dissolved in 130 c.c. (2 mols.) of propionic nhydride at 100°, and 48 g. of sodium propionate (1 mol.) added. The temperature was aised to 160—170° during 15 minutes and maintained for 16 hours; the crystals first formed lissolved after 3 hours. The clear reddish solution was cooled, boiled with 400 c.c. of water,

and, after cooling, the aqueous liquid removed. The heavy brown oil (60 g.) was distilled, and the fraction, b. p. 150—160°/15 mm., collected separately. Yield, 40 g. of a golden-yellow liquid (Found: C, 75·9; H, 5·2. Calc.: C, 75·0; H, 5·0%). 33 G. of the ethylidenephthalide were stirred for 3 days with 50 c.c. of concentrated aqueous ammonia. The reddish-yellow crystalline compound obtained was collected and dissolved in 275 c.c. of alcohol and 75 c.c. of water. The filtered solution deposited 14·6 g. of large yellowish plates, m. p. 209—211°, unchanged by ethylidenephthalimidine prepared by method (b).

(b) A mixture of 130 c.c. of propionic anhydride (2 mols.), 72½ g. of phthalic anhydride (1 mol.), and 56 g. of anhydrous potassium propionate (1 mol.) was heated for 7 hours at 150°, the product boiled with 1 l. of water, and the small oily layer separated. The crystals deposited by the aqueous layer were recrystallised from a mixture of 400 c.c. of glacial acetic acid and 50 c.c. of water, giving 19·3 g. of large crystals of α-phthalidenepropionic acid, m. p. 257—259° (Gabriel and Michael, *loc. cit.*, give m. p. 245—248°) (Found: C, 64·6; H, 3·6. Calc. for $C_{11}H_8O_4$: C, 64·7; H, 3·9%). 8·4 G. of the acid were dissolved in 8 c.c. of concentrated aqueous ammonia and 80 c.c. of water and after 30 minutes the solution obtained was acidified with hydrochloric acid until it was acid to Congo-paper and kept in ice overnight; the white precipitate produced was washed with cold water and dried at 40° (yield, 6·1 g.). 1·1 G., crystallised from 20 c.c. of alcohol, gave 0·5 g. of large clear colourless plates of ethylidenephthalimidine, m. p. 210—212° (Found: C, 76·1; H, 5·7; N, 9·0. Calc. for $C_{10}H_9ON$: C, 75·4; H, 5·7; N, 8·8%). Gabriel and Michael (*loc. cit.*) reported the formation of phthalidenepropionamide, m. p. 193—195°, from ammonia and α-phthalidenepropionic acid by a process similar to that described above.

*Preparation of Benzylidenephthalimidine.*—A vigorous stream of ammonia was passed for 5 hours into 129 g. of molten benzylidenephthalide at 200°. The product separated from glacial acetic acid in heavy yellow crystals (70 g.), m. p. 184—185° (dried at 40°) (Found: C, 81·3; H, 4·5; N, 6·5. Calc. for $C_{15}H_{11}ON$: C, 81·4; H, 5·0; N, 6·4%). A further 35 g. of less pure product were obtained by concentration of the filtrate. Gabriel (*Ber.*, 1885, **18**, 2433) gives m. p. 182—183°.

The author thanks Imperial Chemical Industries, Ltd., and the Directors of the Dyestuffs Group for permission to publish this investigation.

[*Received, October 29th*, 1937.]

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## 2. *Modified Cinchona Alkaloids. Part V. β-*iso*Quinotoxine and the Stereochemistry of the Parent Bases.*

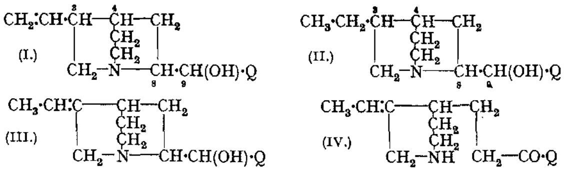
By William Solomon.

The relative configurations of three of the four asymmetric carbon atoms in the cinchona alkaloid molecule are known, and evidence is here adduced in favour of a lævorotatory configuration of the remaining carbon atom.

The principal, naturally occurring, stereoisomeric pairs of cinchona alkaloids (I, II) each have four asymmetric carbon atoms, here numbered 3, 4, 8 and 9 in accordance with the system proposed by Rabe and Riza (*Annalen*, 1932, **496**, 152) and adopted in Part IV of this series (J., 1937, 592). The relative configurations of carbon atoms 8 and 9, as first announced by King and Palmer (J., 1922, **121**, 2577), are known to be dextrorotatory in the dextrorotatory alkaloids cinchonine, quinidine, etc., and lævorotatory in cinchonidine and quinine [Rabe *et al.*, *Annalen*, 1910, **373**, 85; 1932, **492**, 242; Vereinigte Chininfabriken, Zimmer u. Co., G.m.b.H., G.P. 330,813/1918 (experimental work by Rabe's pupil, Fräulein E. Müller)].

The relative dextrorotatory configuration of carbon atom 3 was established in Part IV (*loc. cit.*) by a comparison of the optical rotations of ordinary dihydroquinine and dihydroquinidine (II, Q = 6-methoxy-4-quinolyl) with those of the corresponding $C_8$-epimerides, both pairs in each case being obtained by the catalytic hydrogenation of the *iso*-quinines and -quinidines (III, Q = 6-methoxy-4-quinolyl). Although experimentally applicable only to the methoxylated alkaloids quinine and quinidine, this

configuration of carbon atom 3 must be extended also to the other cinchona alkaloids, which, as has been pointed out by Rabe (*loc. cit.*), all have one and the same configuration



Q = 4-quinolyl or 6-methoxy-4-quinolyl.

at the centres 3 and 4. The dextro-configuration of carbon atom 3 is supported also by a consideration of the optical rotations of α- and β-*iso*quinine (III, Q = 6-methoxy-4-quinolyl). For, both these geometrical isomerides, which may be regarded as quinine (I) in which the asymmetry of centre 3 has been destroyed, have higher lævorotations than quinine itself.

The preparation, and determination of the optical rotation of β-*iso*quinotoxine (IV, Q = 6-methoxy-4-quinolyl) to be described herein, constitute the first evidence of the configuration of carbon atom 4. This substance has been prepared previously by Suszko (*Bull. Inter. Acad. Polonaise,* 1925, *A*, 137), but he did not concern himself with its optical rotation. β-*iso*Quinotoxine is now found to be lævorotatory, and seeing that it has only one centre of asymmetry, carbon atom 4, the asymmetry of the other three centres (3, 8, 9) in this molecule being destroyed, carbon atom 4 must itself be lævorotatory. This evidence, though not conclusive, is of the same nature as that which has for so many years caused carbon atoms 3 and 4 taken together to be considered as dextrorotatory in total effect.

With this proviso, therefore, the stereochemical picture of the cinchona alkaloids is now complete, and may be tabulated as follows :

| Substance. | | Relative configurations at C atoms. 3. | 4. | 8. | 9. |
|---|---|---|---|---|---|
| Cinchonine<br>Dihydrocinchonine<br>Quinidine<br>Dihydroquinidine | dextro-rotatory series | + | − | + | + |
| Cinchonidine<br>Dihydrocinchonidine<br>Quinine<br>Dihydroquinine | lævo-rotatory series | + | − | − | − |

Dr. T. A. Henry, whom I desire to thank for his interest in this work, informs me that he has converted *epi*-$C_3$-dihydroquinine into the corresponding toxine. Although the quantity available is at present too small to enable a complete purification and characterisation of this substance to be made, he has nevertheless succeeded in establishing that it has a pronounced lævorotatory power, a fact which will be readily seen to be in conformity with my own findings concerning the configuration of carbon atom 4.

## Experimental.

β-*iso*Quinotoxine was prepared from β-*iso*quinine by prolonged boiling with dilute acetic acid by the method of v. Miller and Rohde (*Ber.*, 1894, **27**, 1187, 1279; 1895, **28**, 1056).

β-*iso*Quinine (10 g.) was dissolved in 7·5% aqueous acetic acid (200 c.c.), and the pale solution boiled under reflux for 36 hours, either continuously or spread over 5 days. The solution progressively darkened. The base was recovered without loss by means of sodium hydroxide and ethereal extraction. This crude toxine was a dark brown oil. For purification it was converted into the acid tartrate in alcoholic solution, and recrystallised several times, at first from concentrated syrupy alcoholic solution, and finally from 10 parts of alcohol.

The *acid tartrate* so obtained consisted of tiny, loose, cream-tinted needles, m. p. 192—194° (corr., decomp.) after preliminary softening several degrees lower, $[\alpha]_D^{15^\circ}$ −12·0° ($c$ = M/40 in water). It was sparingly soluble in alcohol, but readily in water to give a yellow solution. The salt was anhydrous (Found: C, 61·1; H, 6·4; N, 5·8. $C_{20}H_{24}O_2N_2,C_4H_6O_6$ requires C, 60·7; H, 6·4; N, 5·9%). The base obtained from this salt was a viscous, straw-coloured oil which could not be distilled in a high vacuum; neither could it be crystallised. After drying in a vacuous desiccator over sulphuric acid for 4 weeks, it had $[\alpha]_D^{15^\circ}$ −33·8° ($c$ = M/40 in 0·1N-sulphuric acid). The *neutral tartrate* crystallised from alcohol and resembled the acid salt in appearance, m. p. 162—166° (corr., decomp.), $[\alpha]_D^{15^\circ}$ −12·0° ($c$ = M/40 in water). The air-dried salt contained $2H_2O$ [Found: loss on drying, 5·1. $(C_{20}H_{24}O_2N_2)_2,C_4H_6O_6,2H_2O$ requires $2H_2O$, 4·3%. Found in anhydrous salt: C, 67·0; H, 7·0; N, 6·8. $(C_{20}H_{24}O_2N_2)_2,C_4H_6O_6$ requires C, 66·1; H, 6·8; N, 7·0%]. The *sulphate* separated from 1 or 2 parts of alcohol as a buff-coloured, granular powder, readily soluble in water and in alcohol, m. p. 198—199° (corr., decomp.), $[\alpha]_D^{15^\circ}$ − 25·2° ($c$ = M/40 in water) and − 22·9° in 0·1N-sulphuric acid. The salt contained 3½ $H_2O$ [Found: loss on drying, 7·9. $(C_{20}H_{24}O_2N_2)_2,H_2SO_4,3{\cdot}5H_2O$ requires $3{\cdot}5H_2O$, 7·8%. Found in anhydrous salt: C, 63·9; H, 7·0; N, 7·2; S, 4·5. $(C_{20}H_{24}O_2N_2)_2,H_2SO_4$ requires C, 64·3; H, 6·7; N, 7·5; S, 4·3%].

The author is indebted to Mr. A. W. Stokes for assistance with the experimental work, and to Messrs. A. Bennett and H. C. Clarke for the micro-analyses.

WELLCOME CHEMICAL RESEARCH LABORATORIES,
LONDON, N.W. 1. [*Received, November 18th,* 1937.]

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## 3. *Complexes of Polynitro-compounds. Part II. Compounds of Polynitro-substances with Derivatives of* 1-*Keto*-1 : 2 : 3 : 4-*tetrahydrocarbazole.*

By ANDREW KENT and DONALD MCNEIL.

The capacity of 1-ketotetrahydrocarbazole (K) to provide crystalline termolecular (1 : 2) compounds containing one molecule of certain polynitro-substances (*e.g.*, *m*- or *p*-dinitro- and *s*-trinitro-benzene, picric acid; Part I, J., 1935, 976) is found to be retained in some degree by six of the seven monomethyl homologues (2 to 8). This is apparently the first direct demonstration of a relationship between the constitution of a substance containing only one aromatic system (simple or condensed) and the composition of such ternary molecular compounds with polynitro-materials.

### EXPERIMENTAL.

Suspensions of the appropriate hydroxymethylene *cyclo*ketones (from *cyclo*ketone, ethyl formate and "atomised" sodium) afforded the following phenylhydrazones on treatment with a neutral solution of diazotised amine. When 3-methyl*cyclo*hexanone was used, the yield was poor. The crude products were recrystallised from alcohol: cyclo*hexane*-1 : 2-*dione*-1-m-*tolylhydrazone*, light brown plates, m. p. 156—158° (Found: N, 13·1. $C_{13}H_{16}ON_2$ requires N, 13·0%); cyclo*hexane*-1 : 2-*dione*-1-(6′-*cyano*-m-*tolylhydrazone*), light brown, minute, prismatic needles, m. p. 123° (Found: N, 17·6. $C_{14}H_{15}ON_3$ requires N, 17·4%) (the customary indolising media—hydrochloric acid, acetic acid, dilute sulphuric acid—do not afford a homogeneous product from this compound); cyclo*hexane*-1 : 2-*dione*-2-(4′-*nitrophenylhydrazone*)-1-(6′-*cyano*-m-*tolylhydrazone*), from acetic acid, was obtained on recrystallisation from alcohol as a brown powdery solid (microscopic needle clusters), m. p. 214—215° (Found: N, 22·4. $C_{20}H_{20}O_2N_6$ requires N, 22·3%); cyclo*hexane*-1 : 2-*dione*-1-o-*carboxyphenylhydrazone*, light brown prisms, m. p. 185—186° (Found: N, 11·5. $C_{13}H_{14}O_3N_2$ requires N, 11·4%).

The product obtained as above from 3-methyl*cyclo*hexanone and aniline (heterogeneous crystals, m. p. 190—205°. Found: N, 13·1. $C_{13}H_{16}ON_2$ requires N, 13·0%) was not further investigated prior to indolisation; the reagents there used apparently hydrolysed any 3-methyl-*cyclo*hexane-1 : 2-dione-2-phenylhydrazone which had been added.

4-*Methyl*cyclo*hexane*-1 : 2-*dione*-2-*phenylhydrazone* was obtained in light yellow, rectangular plates, m. p. 139—141° (Found: N, 13·1. $C_{13}H_{16}ON_2$ requires N, 13·0%). It was also obtained

by the Japp–Klingemann reaction (cf. Lions, *Proc. Roy. Soc. N.S.W.*, 1932, **66**, 516) from 4-methyl*cyclo*hexanone-2-carboxylic acid—obtained in poor yield by the method of Gardner, Perkin, and Watson (J., 1910, **97**, 1769)—in salmon-pink plates, m. p. 139—140° (Found: N, 13·1%). Both specimens afforded the same product on indolisation. No evidence of stereoisomerism was obtained.

The 1-keto-tetrahydrocarbazoles desired were, with the exception noted, readily obtained from the appropriate phenylhydrazone in good yield (70—80%) by suitable modification of the procedure given in Part I, but no addition of boiling water was necessary to precipitate the benzo- or carboxy-ketotetrahydrocarbazoles. Of the characteristic *p*-nitrophenylhydrazones prepared in acetic acid from several of these indoles, none retained the capacity of K's *p*-nitrophenylhydrazone (Part I) to combine with alcohol in producing a complex of contrasted colour.

1-*Keto-2-methyltetrahydrocarbazole*-p-*nitrophenylhydrazone* gave brick-red prisms from alcohol, m. p. 226—228° (Found: N, 16·9. $C_{19}H_{18}O_2N_4$ requires N, 16·8%).

1-*Keto-3-methyltetrahydrocarbazole* was obtained in yellowish flat needles, m. p. 194—195°, from acetone (Found: N, 7·1. $C_{13}H_{13}ON$ requires N, 7·0%), in 70% yield. The nature of its picrate (see table) is incompatible with the properties of the salt-like picrates from indolenines (cf. Plancher, *Atti R. Accad. Lincei*, 1900, **9**, I, 221). The p-*nitrophenylhydrazone* gave purple prismatic needles, m. p. 265—267° (darkening), from alcohol (Found: N, 17·0%).

1-*Keto-4-methyltetrahydrocarbazole* was obtained in colourless plates, m. p. 131°, from acetone (Found: N, 7·1%). The p-*nitrophenylhydrazone* gave dark red prisms, m. p. 227—229° (darkening), from alcohol (Found: N, 16·9%).

1-*Ketotetrahydrocarbazole-8-carboxylic acid* was obtained in colourless needles, m. p. 279—281° (sintering at 262°, darkening), from alcohol (Found: N, 6·2. $C_{13}H_{11}O_3N$ requires N, 6·1%). Indolisation of the starting material with 20% sulphuric acid afforded an identical product. The acid was sparingly soluble in hot or cold water. The p-*nitrobenzyl* ester gave small colourless needles, m. p. 189°, from alcohol (Found: N, 7·8. $C_{20}H_{16}O_5N_2$ requires N, 7·7%), and regenerated the original acid on brief (30 mins.) boiling with alcoholic caustic potash (10%).

This acid partly sublimed unchanged above 295°, but some decomposition occurred, accompanied by evolution of carbon dioxide; it was, however, largely unaffected by treatment with quinoline and copper-bronze (sealed tube, 5 hrs. at 310°). When the acid or its sodium salt (colourless needles from moderately concentrated alkali solution; m. p. above 300°) was heated with soda-lime, deep-seated decomposition ensued with the formation of evil-smelling yellow sublimates. Preliminary experiments had shown that 1-ketotetrahydrocarbazole sublimes unchanged at 240—280°. These results, in conjunction with those obtained from the above cyanophenylhydrazone, led to the abandonment of efforts to synthesise directly 1-keto-5-methyltetrahydrocarbazole.

1-*Keto*-5 (or 7)-*methyltetrahydrocarbazole* was obtained (*vide infra*) in colourless plates, m. p. 160—161°, from alcohol (Found: N, 7·2% *).

1-*Keto-6-methyltetrahydrocarbazole*-p-*nitrophenylhydrazone* gave dark red, iridescent plates, m. p. 260° (decomp.), from alcohol (Found: N, 16·8% *).

1-*Keto*-7 (or 5)-*methyltetrahydrocarbazole* was obtained in brownish plates, m. p. 196° (Found: N, 7·2%). This configuration is assigned to the product obtained in small quantity (*ca.* 1 g.) when the hot indolising mixture (7 g. of phenylhydrazone, 42 c.c. of acetic acid, and 7 c.c. of concentrated hydrochloric acid) was treated with successive small quantities of boiling water. The residual solids (m. p. 125—140°. Found: N, 7·1%) could not be further separated by fractional crystallisation from alcohol, acetone, or acetic acid. Alternatively, by complete precipitation of the indolised materials (m. p. 150—190°. Found: N, 7·2%), followed by recrystallisation from alcohol and treatment of their solution in alcohol (60 pts.) with picric acid (0·5 mol.), the picrate of the 7 (or 5)-isomer (see table) was obtained in 10% yield, and a similar further quantity resulted from cautious concentration of the filtrate. The residual mixed picrates could not be resolved by fractionation; but during one attempt with aqueous alcohol hydrolysis took place in such a manner as to precipitate the 5 (or 7)-isomer (0·1 g.), m. p. 157—160° [mixed m. p. with the 7 (or 5)-isomer, 130—143°].

The following *molecular compounds*, all of which appear to be new, were best prepared from an appropriate concentration of the components in the solvent indicated; they were, where practicable, recrystallised from that solvent before analysis. Those formed from *s*-trinitrobenzene (X), picric acid (Y), or *m*-dinitrobenzene (Z) compare directly with the analogous complexes $XK_2$, $YK_2$, $ZK_2$ described in Part I. Alternative figures for nitrogen analyses are derived from separate preparations.

| Poly-nitro-component. | Amino-component. | Complex. | N, %. Found. | N, %. Calc. | Description. | M. p. | Solvent. |
|---|---|---|---|---|---|---|---|
| X | A. 2-Methyl-K | XA | 13·7 13·8 | 13·6 | Canary-yellow needles | 180° | $C_2H_5$·OH (1 : 1 soln.) |
| ,, | ,, | $XA_2$ | 11·6 11·5 | 11·45 | Golden-yellow prismatic needles | 186—187 | $C_6H_6$ (1 : 1 or 1 : 2 soln.) |
| Y | ,, | $YA_2$ | 11·3 11·2* | 11·2 | Orange-yellow felted needles | 154—155 | $C_2H_5$·OH |
| X | B. 3-Methyl-K | $XB_2$ | 11·5 | 11·45 | Golden-yellow needles | 187—188 | ,, |
| Y | ,, | $YB_2$ | 11·5 | 11·2 | Orange-red needles | 169 | $C_6H_6$ |
| X | C. 4-Methyl-K | $XC_2$ | 11·6 | 11·45 | Deep golden-yellow needles | 177 | $C_2H_5$·OH |
| Y | ,, | $YC_2$ | 11·2 | 11·2 | Red flat needles | 157—159 | ,, |
| X | D. 5 (or 7)-Methyl-K | $XD_2$ | 11·5* | 11·45 | Orange-yellow felted needles | 190—192 | ,, |
| Y | ,, | $YD_2$ | 11·2* | 11·2 | Orange-red prismatic needles | 158—159 | ,, |
| X | E. 6-Methyl-K | XE | 13·5* | 13·6 | Yellow fluffy needles | 174—176 | ,, |
| Y | ,, | YE | 13·1* | 13·1 | Buff minute needles | 156—158 | ,, |
| Z | ,, | ZE | 11·4* | 11·45 | Yellow stiff needles | Incongruent | ,, |
| X | F. 7 (or 5)-Methyl-K | $XF_2$ | 11·7* | 11·45 | Orange-yellow fine needles | 201—203 | ,, |
| Y | ,, | $YF_2$ | 11·1* 11·2 | 11·2 | Orange-red plates | 183 | ,, |
| X | G. 8-Methyl-K | XG | 13·7 13·7 | 13·6 | Golden-yellow felted needles | 179—180 | ,, |
| Y | ,, | YG | 13·2 | 13·1 | Orange-red needles | 161—162 | ,, |
| Z | ,, | $ZG_2$ | 9·9* 9·8* | 9·9 | Yellow plates | Incongruent | $C_2H_5$·OH + $m$-$C_6H_4(NO_2)_2$ |
| X | P. 5 : 6-Benzo-K | XP | 12·7 | 12·5 | Yellow fibrous needles | 229—231 | $CH_3$·$CO_2H$ |
| Y | ,, | YP | 12·2 | 12·1 | Light-red fibrous needles | 212—214 (decomp.) | ,, |
| X | Q. 7 : 8-Benzo-K | XQ | 12·3 | 12·5 | Bright yellow needles | 240—241 | ,, |
| Y | ,, | YQ | 12·1 | 12·1 | Red needles | 220—222 (decomp.) | ,, |

In preliminary investigations 1 : 1 solutions of the components were generally used. Following filtration of the solid complex and concentration of the mother-liquor, evidence suggestive of the composition later confirmed by analysis was readily obtained.

A 1 : 2 solution of X and A in absolute alcohol precipitated $XA_2$ with a few crystals of the XA type: this heterogeneous solid rapidly became homogeneous $XA_2$ (Found: N, 11·6%) in contact with the liquor. In no other instance was evidence obtained that variation in solvent or in relative concentration of components could produce alternative molecular compounds.

$YB_2$ or ZE, and especially the latter, gave visible evidence of partial dissociation into their colourless components on attempted recrystallisation from dilute alcoholic solution. $ZG_2$, even from concentrated alcoholic solution, precipitated only its components, unless some additional Z, recoverable from the mother-liquor after filtration, had been introduced before crystallisation began.

Although coloured crystals were visible, the precipitate from a 1 : 1 or 1 : 2 alcoholic solution of Z and A was clearly contaminated by uncombined material. Neither E nor G provided coloured precipitates when dissolved with $p$-dinitrobenzene in absolute alcohol.

Analysis of coloured complexes was invariably preceded by examination of the specimen's homogeneity under a low-power microscope. Micro-analyses (N*) were conducted by Mr. J. M. L. Cameron.

XG and YG resemble $XK_2$ and $YK_2$ in recrystallising unchanged from benzene, and Dr. G. Thomson very kindly undertook the following molecular-weight determinations (cryoscopic method) of the amino-component:

| Compound. | *c* (g./100 g. $C_6H_6$). | *M* (found). | Formula wt. |
|---|---|---|---|
| K | 0·909, 1·22 | 211·5, 219 | 185 |
| G | 0·883, 1·24 | 282·4, 282·1 | 199 |

### DISCUSSION.

The molecular compounds of this series show no standard concomitant (*e.g.*, colour, stability) of variation in composition. With two exceptions ($XB_2$, and notably XE) the derivatives of *s*-trinitrobenzene melt at a higher temperature than either constituent: and the more deeply coloured picrates melt consistently at a somewhat (24° ± 7°) lower temperature than the analogous derivatives of X (cf. Pfeiffer, "Organische Molekülverbindungen," Stuttgart, 1927, p. 357).

Some evidence has already been offered (Part I) against the possibility that ternary complex-formation in this series results from prior association of the component amine; and the molecular-weight determinations now provided indicate a negative correlation between degree of association and facility in production of crystalline ternary derivatives.

Crystalline convenience has been suggested (Bennett and Wain, J., 1936, **1115**) as a primary factor in ternary complex-formation of an apparently erratic type like 1 β-naphthol : 2 tetramethylphthalan; but this appears inapplicable to a series of such high consistency as the above (cf. Lowry, *Chem. and Ind.*, 1924, **43**, 220).

It seems reasonable, therefore, to assume that such ternary complex-formation by K and its homologues is achieved by duplication of whatever mechanism is involved in the formation of the normal binary type. The isolation of XA and $XA_2$ suggests that in solutions of suitable materials both types are present in characteristic ratios which may, on occasion, permit isolation of either by variation of solvent and/or concentration (cf. alternative 2 : 1 and 1 : 1 types; Sudborough, J., 1916, **109**, 1342).

It is clear on the other hand (cf. $XK_2$, XE, XP) that crystalline ternary complex-formation cannot be predicted with confidence on constitutional grounds (cf. the ternary complex of *s*-trinitrobenzene with benzene; Hammick, Hills, and Howard, J., 1932, 1530, and its binary complexes with toluene, etc.; Pfeiffer, *Annalen*, 1917, **412**, 297).

The effect, on crystalline complex-composition, of an additional nitro-group in $ZG_2$ and XG resembles that exhibited in the corresponding compounds of 4 : 4'-bisdimethylaminodiphenylmethane (Romburgh, *Rec. trav. chim.*, 1888, **7**, 228) and in other complexes of K [Part I, cf. compound (c) or (d) with (b)].

The authors thank Mr. R. S. Allison for supplies of the compounds E, F, and G, and one of them (D. McN.) further acknowledges with gratitude the tenure of a Donaldson Scholarship from this University, and of a Carnegie Scholarship.

UNIVERSITY OF GLASGOW. [*Received, June 14th*, 1937.]

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## 4. *Mechanism of Polymerisation. Part II. Dimerisation of βγ-Dimethylbutadiene in Presence of an Acid Catalyst.*

By ERNEST HAROLD FARMER and ROBERT C. PITKETHLY.

Polymerisation of βγ-dimethylbutadiene by sulphuric acid dissolved in acetic acid gives dimeric, trimeric and other low-molecular products, but the nature of the product varies somewhat with the experimental conditions.

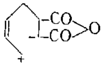
The dimeric product consists mainly of a monocyclic (*cyclo*hexenic) hydrocarbon, but under suitable conditions a solid, camphor-like (dicyclic) dimeride is also formed. There is evidence also that the *cyclo*hexenic dimeride is contaminated by a third liquid (dicyclic) dimeride.

The *cyclo*hexenic dimeride is identical with that which has frequently been obtained by the action of heat on βγ-dimethylbutadiene, but Lebedev's preparation of the latter appears to have contained also a fourth (dicyclic) dimeride. The *cyclo*hexenic dimeride has been synthesised.

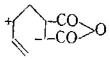
The formation of both monocyclic and dicyclic dimerides, as also the formation of the *cyclo*pentenic dimeride obtainable from α-phenylbutadiene, is readily representable on the basis of Whitmore's hypothesis.

LITTLE is known at present as to how many courses of reaction even the simplest of *low-molecular* polymerisation processes can follow. In the case of *high-molecular* polymerisations, according to the Staudinger conception, reaction both for olefins and for conjugated diolefins pursues normally a uniform course with formation of products which in a given example differ only in the degree of polymerisation (and hence in the chain length of the molecules) attained; and even in those examples where uniform head-to-tail arrangement of the molecules seems to be disturbed by some degree of 1 : 2- or of head-to-head/tail-to-tail linking, the habit of forming essentially linear "polymer-homologous" products is retained. But with low-molecular polymerisations there is little information as yet to show whether reaction promoted by heat necessarily yields the same product or products at each polymeric stage as reaction promoted by chemical reagents or by electric discharge, nor has the range of isomerism which can occur with any particular polymerising agency at the different polymeric stages beeu determined.

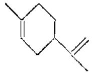
The published evidence at the time this investigation was begun indicated that conjugated diene hydrocarbons yielded on polymerisation either low-molecular products which consisted mainly or wholly of cyclic dimerides, or high-molecular products which were more or less rubber-like in character. It seemed that the formation of the dimeric substances, whether promoted by heat or by catalysts, followed invariably a single course, *viz.*, one which was formally analogous to the Diels–Alder reaction between conjugated dienes and maleic anhydride. Consideration, however, of the analogy between the two types of additive reaction led to the conclusion that the resemblance between the reactions could only be purely superficial in character, since the Diels–Alder reaction with little doubt depended for its initiation on the dissimilar polar character of the reactants [anionoid hydrocarbon and kationoid addendum as suggested by R. Robinson, "Outline of an Electrochemical (Electronic) Theory of the Course of Organic Reactions," p. 29], whereas in the dimerisation reaction no pronounced tendency to interaction on the part of two hydrocarbon molecules, *both* normally anionoid, could be envisaged, unless activation of one of the molecules had supervened whereby its polar character became altered. By the normal mechanism of the Diels–Alder reaction as pictured by Robinson the formation of only *cyclo*hexene- or alkenyl*cyclo*butane-derivatives could be expected, since the first stage of addition would yield an open-chain polar complex such as (I) or (II) (from butadiene and maleic anhydride); and present experience shows that the *cyclo*hexenic compounds



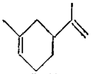

(I.)




(II.)



(III.)



(IV.)

are invariably the favoured products.* Departure, however, from the Diels–Alder mechanism at once removes this restriction on the form of the dimeric products and opens up the possibility of the formation of either open-chain or cyclic compounds, the latter of which may be *cyclo*hexenic, *cyclo*pentenic or conceivably *cyclo*butenic in character.

With the foregoing possibilities in view work was initially begun by one of us with Mr. H. Brunner on the low-molecular polymerisation of β-phenylbutadiene. The work on the constitution of the dimeric constituent of the low-molecular product, which was a re-examination of the earlier results of Lebedev (*Chem. Zentr.*, 1914, i, 1407; 1923, i, 1539), was, however, forestalled by Bergmann (J., 1935, 1359), who showed that Lebedev's *cyclo*hexenic formula for the dimeride was incorrect and the latter had in fact a *cyclo*pentenic constitution. This result (although we reject Bergmann's tentative suggestion as to the mechanism of reaction) fulfilled at once one of the expectations set out above,

* On the other hand, in the apparently analogous additions of diphenylketen to conjugated olefins, four-carbon rings seem to be the rule.

*viz.*, that the *cyclo*hexenic form was not a necessary consequence of dienic dimerisation. The following results connected with the low-polymerisation of βγ-dimethylbutadiene not only serve to confirm the distinctive natures of the Diels–Alder and the dimerisation reactions but throw new light on the mechanism of reaction.

*Polymerisation by the Bertram–Walbaum Reagent.*—Hydration of compounds containing isolated double bonds has often been effected by sulphuric acid in acetic acid since this reagent was first introduced by Bertram and Walbaum. The only previously recorded instance of its action on conjugated dienes, however, is due to Wagner-Jauregg (*Annalen*, 1932, **496**, 52), who transformed isoprene into a complex mixture of products containing two *cyclo*hexenic dimerides (III) and (IV) in addition to trimeric material (apparently partly monocyclic) and various mono- and sesqui-terpenic alcohols. The complexity of Wagner-Jauregg's product suggested the necessity for a detailed investigation of the simplest diene, *viz.*, butadiene, but its relative inaccessibility in pure form made it more practicable to study βγ-dimethylbutadiene, the symmetrical structure of which restricts the possibilities of isomerism in the products of polymerisation. The relative polymerisabilities of butadiene, isoprene, and βγ-dimethylbutadiene are indicated in Table I, and are in agreement with those expected on constitutional grounds.*

TABLE I.

*Polymerisation of Dienes (Bertram–Walbaum Reagent).*

| | Conc. of $H_2SO_4$ in reagent. | Time (days). | Extent of polymerisation (%). | | Conc. of $H_2SO_4$ in reagent. | Time (days). | Extent of polymerisation (%). |
|---|---|---|---|---|---|---|---|
| Butadiene ... | 4 | 3 | 25 | βγ-Dimethylbutadiene | 0·1 | 3 | 44 |
| ,, ... | 4 | 9 | 58 | ,, | 0·1 | 4 | 57 |
| Isoprene † ... | 0·3 | 3 | 30 | ,, | 1 | 4 | 85 |
| | | | | ,, | 4 | 4 | 90 |

† Figures due to Wagner-Jauregg (*loc. cit.*).

The products of the polymerisation of βγ-dimethylbutadiene with the Bertram–Walbaum reagent were freed from alcohols and then subjected to systematic fractional distillation, and Table II shows that the composition of the polymerisation mixture varied with the concentration of sulphuric acid in the reagent. The present communication is concerned only with the study of the dimeric products, and it was found that, whereas the use of 0·1% sulphuric acid in acetic acid led to an apparently homogeneous terpenic liquid dimeride, when the concentration was 1% there was formed a similar but not entirely homogeneous terpenic liquid dimeride (showing appreciable variations in the physical properties of its fractions on distillation) as well as a camphor-like solid dicyclic dimeride (1·5% yield) the constitution of which is being investigated. Very narrow limits of concentration are requisite for the formation of this solid dimeride, which, moreover, could not be obtained at will by the action of sulphuric acid on the liquid dimeride.

TABLE II.

*Variation in Composition of Polymerisation Products.*

| Concn. of $H_2SO_4$ (%). | Vol. (c.c.) of reagent per g. of hydrocarbon. | Time (days). | Total yield (%). | Composition. | | |
|---|---|---|---|---|---|---|
| | | | | Dimeride (%). | Trimeride (%). | Higher polymerides (%). |
| 0·1 | 3·0 | 4 | 56 | 52 | 34 | 14 |
| 1 | 4·4 | 4 | 93 | 28 | 24 | 43 |
| 4 | 13·6 | 4 | 95 | 19 | 35 | 44 |

*Constitution of the liquid dimeride.* The liquid dimeride obtained by the use of low concentrations of sulphuric acid (about 0·1%) was doubly unsaturated, as was shown by quantitative additive experiments with bromine, hydrogen chloride, and hydrogen. The addition compounds were liquid, as also were those resulting from the action of nitrosyl

* Experiments made several years ago by Mr. R. G. R. Bacon show that αγ-dimethylbutadiene polymerises as readily as, and αδ-dimethylbutadiene considerably less readily than, βγ-dimethylbutadiene in a reagent containing 0·3% of $H_2SO_4$.

chloride, nitric oxide, and nitrogen peroxide. Saturation of the two double bonds by hydrogen occurred at markedly different rates, so that a dihydride could be isolated in substantially pure condition. The dibromide of this dihydride deposited 12% of an easily decomposed, crystalline dibromide, m. p. 57°, probably one of the four possible stereoisomeric dibromides.

The additive reactions of the liquid dimeride, apart from the isolation of the dihydride and its dibromide, have been described previously for the liquid dimeride obtained by thermal polymerisation of βγ-dimethylbutadiene (five authors) and by heat-degradation of dimethylbutadiene-rubber (Richards). The physical constants of the thermal dimerides, together with those of our material, are cited in Table III, from which it is seen that, although the values for the different preparations show appreciable variations, those for our dimeride obtained with 0·1% sulphuric acid agree with the values observed by Kogerman and by Lebedev, although the latter author had been able to obtain only a monohydrochloride.

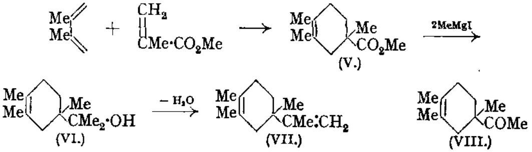
TABLE III.

*Dimeric βγ-Dimethylbutadiene.*

| Author. | Origin. | B. p. | $d_{4^\circ}$. | $n_D$. |
|---|---|---|---|---|
| Dalecki [1] | Heat-formed | 203·5—205·5°/749 mm. | 0·8628$^{19°}$ | — |
| Richards [2] | ,, | 205/760 mm. | 0·8532$^{25°}$ | 1·47786$^{25°}$ |
| Lebedev [3] | ,, | 205/750 mm. | 0·8597$^{20°}$ | 1·48074 |
| Aschan [4] | ,, | 200·5—201·5/760 mm. | 0·8535$^{20°}$ | 1·47915$^{20°}$ |
| Whitby and Crozier [5] | ,, | 198—200/738 mm. | — | 1·4775$^{25°}$ |
| Kogerman [6] | ,, | 205—206/738 mm. | 0·8592$^{20°}$ | 1·48107$^{20°}$ |
| Present authors | Acid-formed | 85/15 mm. | 0·8585$^{22°}$ | 1·4804$^{22°}$ |
| ,, ,, | Synthetic | 206·5—207·5/760 mm. | 0·8626$^{16°}$ | 1·4823$^{16°}$ |

[1] *J. Russ. Phys. Chem. Soc.*, 1903, **35**, 533. [2] *Compt. rend.*, 1911, **153**, 116. [3] *J. Russ. Phys. Chem. Soc.*, 1913, **45**, 1249, 1379. [4] *Oversikt. Finsk. Vetenskaps. Soc. Forh.*, 1915, **58**, 42; *Chem. Abs.*, 1920, **14**, 3823. [5] *Canadian J. Res.*, 1932, **6**, 218, 280. [6] *Sitzungsber. Naturforsch. Ges. Tartu*, 1935, **41**.

Thus it appears that the dimerides formed by heat- and by acid-treatment are identical as regards the main constituent, a view which is supported by the fact that our hydrocarbon resembled that of Kogerman in undergoing selenium dehydrogenation to an aromatic hydrocarbon (probably 3 : 4-dimethylcumene) which could be oxidised to trimellitic acid. These observations are consistent with the view that the principal dimeric compound has the structure (VII). Confirmation of this view was afforded by the synthesis of (VII) from βγ-dimethylbutadiene and methyl α-methylacrylate according to the scheme:

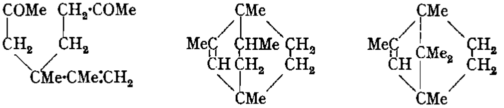



The intermediate ketone (VIII) and a compound $C_{13}H_{24}O$, probably the methyl ether of (VI), were among the by-products of the Grignard condensation. The physical and chemical properties of the synthetic hydrocarbon (VII) resemble closely those of the acid-formed dimeride of βγ-dimethylbutadiene and also the thermal dimeride of Lebedev and of Kogerman (see Table III).

Lebedev reported that his thermal dimeride of βγ-dimethylbutadiene was oxidised by permanganate to a diketone (IX) (about 30% yield), which gave a disemicarbazone, m. p. 228°. Kogerman, on the other hand, obtained formaldehyde by ozonolysis of his dimeride, but could not isolate or identify the major degradation product. Our acid-formed dimeride behaved similarly to Kogerman's compound and gave on ozonolysis a 70% yield of formaldehyde together with a yellow oil from which no solid ketone deriv-

ıtives could be obtained. By permanganate oxidation we obtained a substantial yield ›f formic acid together with a neutral product which consisted partly of unattacked ıydrocarbon but contained *inter alia* some proportion of a dicarbonyl derivative; the atter gave in small yield a disemicarbazone of the same empirical formula as Lebedev's :ompound, but of different melting point (m. p. 251°).

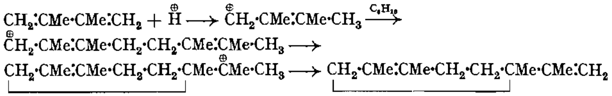
The formation of a diketone of formula (IX) from the dimeride (VII), involving as t does attack at the endocyclic double bond in preference to the exocyclic one, is not redible in view of the foregoing observations and of general experience. We therefore onclude from the evidence adduced above that none of the specimens of dimeride is com›letely homogeneous, but they consist mainly of (VII). We have little doubt that the arge proportion of diketone formed by oxidation of Lebedev's dimeride and the small ımount of an isomeride from ours arose by fission of mono-olefinic dicyclic compounds * or which the formula (X) (2 stereo-forms), or formulæ (X) and (XI) are tentatively uggested.

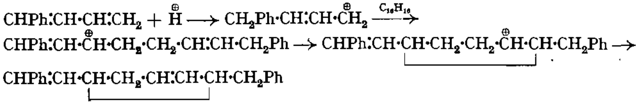


(IX.) (X.) (XI.)

'aughan (*J. Amer. Chem. Soc.*, 1932, **54**, 3868; 1933, **55**, 4009) has already suggested, ›ithout adducing convincing evidence, that dicyclic forms may accompany the ordinary *yclo*hexenic dimeride in heat-polymerised butadiene.

The formation of the monocyclic and dicyclic dimerides, like that of the *cyclo*pentenic imeride of α-phenylbutadiene referred to above, can readily be represented on the basis f the Whitmore hypothesis: thus the formation of the first of these may be represented ı scheme (A) and that of the last in scheme (B):

A) 

B) 

EXPERIMENTAL.

*Polymerisation of βγ-Dimethylbutadiene with the Bertram–Walbaum Reagent.—With a* 0·1% *agent.* The hydrocarbon, prepared by dehydration of pinacol hydrate (Kyriakides, *J. Amer. hem. Soc.*, 1914, **36**, 987), was washed with water, dried over calcium chloride, and rectified ıder a Widmer column (b. p. 69°/760 mm.) just before use. A portion (160 g.) was dissolved the reagent (500 c.c.) containing 0·1 g. of concentrated sulphuric acid per 99·9 g. of glacial :etic acid. After 96 hours the solution was stirred into $1\frac{1}{2}$ l. of water, and the product exacted with ether. The extract was washed with sodium carbonate solution until neutral ıd with water, dried over anhydrous sodium sulphate, and freed from solvent under a metreng Vigreux column and from unchanged dimethylbutadiene (10 g.) by partial distillation ıder a shorter column. The residual oily liquid (96 g.; 64%) was refluxed for 4 hours with ı-methyl-alcoholic potassium hydroxide (500 c.c.); most of the alcohol was then distilled, ıd the residue poured into water. The hydrolysis product was extracted in ether, dried

* The fact that Lebedev's dimeride would not combine with 2 mols. of hydrogen chloride (see above) a further indication of the (substantially) dicyclic character of his product.

(sodium sulphate), freed from solvent, heated on a steam-bath for 4 hours with boric acid (20 g.), and finally divided into the following fractions by distillation: (i) 60—120°/20 mm. (47 g.; colourless), (ii) 120°/20 mm.—120°/1 mm. (35 g.; faint yellow), (iii) 120—140°/1 mm. (6 g.; yellow), (iv) yellow viscous residue.

The residue was basified with sodium hydroxide and steam-distilled: a fragrant oil (0·5 g.), consisting of the alcohols formed by the Bertram–Walbaum reagent, distilled.

The fraction (i) on redistillation from a Kon flask passed over between 84° and 110° at 24 mm., the b. p.–% distilled curve showing its extensive heterogeneity: reasonably good fractionation could only be achieved by redistillation under a metre-long vacuum-jacketed column, packed with a spiral of copper foil and fitted with a still-head suitable for controlling the reflux-ratio; an apparently homogeneous dimeric *product*, b. p. 85°/15 mm., $n_D^{22°}$ 1·4804, $d_0^{22°}$ 0·8604, was then obtained [Found: C, 87·5; H, 12·1. $(C_3H_5)_2$ requires C, 87·7; H, 12·25%]. The trimeric and higher fractions were saved for subsequent fractionation.

*With a* 1% *reagent.* A solution of the hydrocarbon (204 g.) in 660 c.c. of a Bertram–Walbaum reagent containing 1% (w/w) of concentrated sulphuric acid was kept for 4 days. The polymerisation product, isolated as before, was a brown mobile liquid which contained no unchanged hydrocarbon. It was refluxed for 1 hour with 7½% (w/w) methyl-alcoholic potassium hydroxide and kept for 24 hours, and the hydrolysis product then worked up as before. The oil obtained (191 g.) was heated on a steam-bath with boric acid (20 g.) for 3 hours and then distilled. The following fractions were collected: (i) 45—75°/20 mm., (ii) 75—120°/20 mm., (iii) 120°/20 mm.—120°/1 mm., (iv) 120—165°/1 mm., and (v) a brown viscous residue.

Fraction (ii) was divided into small fractions by distillation in a specially-constructed vacuum-jacketed column, 40 cm. long, and fitted with a reflux still-head allowing of close control of the reflux-ratio. The column was packed with a single spiral of 16-gauge nichrome wire. The lowest fractions which distilled solidified almost completely when cooled in a freezing mixture. The solid was collected on a cooled sintered-glass filter, drained on a tile, and crystallised from methyl alcohol. The crystals, camphor-like in odour, volatilised rapidly on exposure to air; when distilled on to a cold surface, they gave feathery crystals, m. p. 66° (yield, 1·5 g. or 1·6%). This substance was a *dimeride* of dimethylbutadiene [Found: C, 87·9; H, 12·25; *M* (in benzene), 167, 165. $(C_6H_{10})_2$ requires C, 87·7; H, 12·25%; *M*, 164]. The liquid dimeric material from which the solid had been removed was separately rectified; the final product seemed to be slightly less homogeneous than that from the preceding preparation, as judged by the larger range of boiling point and refractive index.

The trimeric fraction (iii) was intensively refractionated, the above-mentioned packed column being used. Since the thermometer at the head of the column gave no indication of the changing composition of the fractions, refractive index–% distilled curves were plotted after each distillation. The fraction corresponding to the flat portion of the curve in the sixth distillation was selected for subsequent work with *trimeric* βγ-*dimethylbutadiene* [Found: C, 87·8; H, 12·2. $(C_6H_{10})_3$ requires C, 87·7; H, 12·25%]: it had $n_D^{24·5°}$ 1·49345, $d_{0°}^{24·5°}$ 0·8953, $[R_L]_D$ 80·04 (calc. for $C_{18}H_{30}|\overline{_2}$, 79·99).

*The Liquid Dimeride.—Hydrogenation.* In ethyl alcohol with Adams's platinum catalyst reaction ceased when 0·3247 g. of the dimeride had absorbed 48·46 c.c. of hydrogen at 17°/764 mm. This corresponds to an unsaturation of 0·99 double bond per $C_{12}H_{20}$-unit. In acetic acid, with the same catalyst, there was a well-marked break at the point corresponding exactly to the absorption of 1 mol. of hydrogen per mol. of dimeride, but reaction only ceased when 2 mols. of hydrogen had been absorbed. The unsaturation values found at the two stages corresponded to 0·99, 1·01 and 2·03, 2·00 double bonds per $C_{12}H_{20}$-unit respectively.

The half-hydrogenated dimeride obtained by reducing 10 g. of the dimeride in 250 c.c. of rectified spirit (catalyst 0·2 g.) was not homogeneous: it gave on rectification under a short column the fractions: (i) 80—86° (0·9 g.), (ii) 86—91° (1·0 g.), (iii) 91—94° (3·9 g.), and (iv) 94—95° (2·0 g.), of which the third (2 g.) gave with bromine (1 mol.) in carbon disulphide a liquid dibromide. From the latter, after two months, a solid dibromide (0·5 g.; 12·7%) separated This formed feathery needles, m. p. 57°, from light petroleum (Found: Br, 49·6. $C_{12}H_{22}Br_2$ requires Br, 49·05%). Presumably the solid and the liquid are stereoisomeric forms of 1 : 2-*dibromo*-1 : 2 : 4-*trimethyl*-4-iso*propyl*cyclo*hexane*.

The fully-hydrogenated dimeride, 1 : 2 : 4-*trimethyl*-4-iso*propyl*cyclo*hexane*, obtained in small amount by reduction of the dimeride in acetic acid solution, was also obtained by heating the dimeride (12·5 c.c.) with concentrated hydriodic acid (17 c.c.) and red phosphorus (1 g.) at 250° for 9 hours. The turpentine-like hydrocarbon, after refluxing over sodium, distilled

mainly between 125° and 132°; after fractionation it was obtained as a mobile liquid, b. p. 177° (Found: C, 85·55; H, 14·55. $C_{12}H_{24}$ requires C, 85·6; H, 14·4%). It had $n_D^{20°}$ 1·4636, $d^{20°}$ 0·8375, $[R_L]_D$ 55·42 (calc., 55·42).

*Dibromide.* When treated with bromine by the method of Rosenmund and Kuhnhenn (*Z. Unters. Nahr. Genussm.*, 1923, **46**, 154), the dimeride absorbed the equivalent of 2 mols. of bromine (unsaturation value 81·75, 81·45. $C_{12}H_{20}|\overline{_2}$ requires 82·15). When bromine (2 mols.) was added to the dimeride in ether–amyl alcohol (method of Baeyer and Villiger, *Ber.*, 1894, **27**, 448), in chloroform, or in carbon disulphide, the bromine was completely absorbed but only a liquid bromide was formed; in ether, hydrogen bromide was evolved and more than 2 mols. of bromine were taken up.

*Dihydrobromide.* An ethereal solution of the dimeride at − 15° was saturated with dry hydrogen bromide (phosphoric oxide). A heavy brown oily layer separated and afterwards redissolved. The product, after being freed from ether by a current of dry air, gave an oily dihydrobromide (1·410 g. of dimeride absorbed 1·36 g. of hydrogen bromide. Calc. for $C_{12}H_{20}|\overline{_2}$, 1·39 g.), from which no solid component could be obtained.

An exactly similar result was obtained when hydrogen chloride replaced hydrogen bromide (1·83 g. of dimeride absorbed 0·94 g. of hydrogen chloride. Calc. for $C_{12}H_{20}|\overline{_2}$, 0·95 g.).

*Nitrosate.* The nitrosate formed by means of amyl nitrite and acetic acid was a yellow oil.

*Dehydrogenation.* Heated with powdered selenium at 280—300° for 21 hours, the dimeride gave principally a yellow oil, b. p. 160—170°: this on boiling for 8 hours with excess of 3% permanganate solution containing sodium carbonate gave, on being worked up, a solid acid, m. p. 206—209°, and 217—218°, after several crystallisations from ethyl acetate. This acid was identified as trimellitic acid, m. p. 219°, mixed m. p. 217—218°; equiv., 70·1, 70·45 (Calc. for $C_9H_6O_6$, 70·05).

*Ozonolysis.* The dimeride (1 g.) was ozonised in pure chloroform (90 c.c.) which itself gave no formaldehyde when successively treated with ozone and water. The colourless solution was refluxed with water for 18 hours; the chloroform layer was then washed with water, dried and freed from solvent by evaporation. The clear yellow oil obtained, when treated *without distillation* with semicarbazide hydrochloride and sodium acetate, yielded no semicarbazone. The aqueous liquor and washings gave 0·7 g. (70% yield) of formaldehyde-2 : 4-dinitrophenylhydrazone, m. p. (after one crystallisation from alcohol) and mixed m. p. 162°.

*Oxidation.* To the dimeride, suspended in water and vigorously stirred, a solution of potassium permanganate (32 g. in 1070 c.c. of water) was slowly added. The mixture, after standing overnight, was just decolorised with sulphurous acid and then worked up in the usual way. The neutral product of the oxidation was carefully fractionated: examination of the fractions showed it to be composed largely of the unchanged dimeride, but partly of a substance of lower specific refractivity than the latter. Treatment of the fractions with semicarbazide acetate gave very slowly and in small yield gritty crystals of a semicarbazone. This was the *disemicarbazone* of a dicarbonyl compound, $C_{12}H_{20}O_2$, the latter being with little doubt derived by fission of the double bond in a dicyclic form of the dimeride (see p. 15) (Found: C, 53·95; H, 8·4. $C_{14}H_{26}O_2N_6$ requires C, 54·2; H, 8·4%).

The aqueous mother-liquor was shown by numerous tests and derivatives to contain a considerable quantity of formic acid.

### *Synthesis of Liquid Dimeride.*

*Addition of Methyl α-Methylacrylate to βγ-Dimethylbutadiene.*—Methyl α-methylacrylate (b. p. 100°) was obtained in 40% yield by the action of concentrated sulphuric acid on acetone cyanohydrin in presence of copper powder. The ester (65 g.), mixed with the hydrocarbon (65 c.c.), was heated in sealed tubes for 4 hours at 150°. The colourless viscous product, when distilled at 20 mm., gave the fractions of b. p. (i) below 26° (16 g.), (ii) 26—100° (1 g.), (iii) 101—104°, but mostly 102—102·5° (70 g.), and (iv) a residue (18 g.). Fraction (i), when reheated with a further 16 c.c. of hydrocarbon, gave 20 g. of the product of b. p. 101—104°; this was combined with fraction (iii), and the whole redistilled from an Adams flask. Practically the whole passed over at 104·5°/20 mm., with no significant variation in the refractive index, to give a colourless mono-olefinic liquid, b. p. 106°/19 mm. (corr.), $n_D^{16°}$ 1·4679, $d_{4°}^{16°}$ 0·9738, $[R_L]_D$ 52·07 (calc., 51·98), unsaturation value, 179·3 (calc., 182·3). This was *methyl* 1 : 3 : 4-*trimethyl-Δ³-tetrahydrobenzoate* (V) (Found: C, 72·6; H, 10·0. $C_{11}H_{18}O_2$ requires C, 72·5; H, 9·95%). 1 : 3 : 4-*Trimethyl-Δ³-tetrahydrobenzanilide*, formed from this ester by the method of Hardy (J., 1936, 398), crystallised from methyl alcohol in colourless needles, m. p. 94·5° (Found: C, 78·9; H, 8·7. $C_{16}H_{21}ON$ requires C, 79·0; H, 8·7%). 1 : 3 : 4-*Trimethyl-Δ³-tetrahydro-*

*benzoic acid*, obtained by refluxing the ester for 3 hours with 10% excess of alcoholic sodium hydroxide, formed colourless leaflets, m. p. 56°, from alcohol or dilute acetic acid (Found: C, 71·0; H, 9·5. $C_{10}H_{16}O_2$ requires C, 71·35; H, 9·6%).

*Ozonolysis of Methyl 1 : 3 : 4-Trimethyl-$\Delta^3$-tetrahydrobenzoate.*—When the ester (2·5 g.) was ozonised in purified ethyl acetate for 5½ hours at 0°, and the product refluxed overnight with water (50 c.c.), the aqueous layer obtained gave no precipitate with 2 : 4-dinitrophenylhydrazine, whereas the ethyl acetate layer yielded, on drying and removal of the solvent, 2 g. of a golden-yellow oil, b. p. 120—170°/14 mm. This gave with semicarbazide hydrochloride and sodium acetate solution 2 g. of the *disemicarbazone* of methyl α-acetonyl-γ-acetyl-α-methylpropionate, m. p. 200° after recrystallisation from aqueous alcohol (Found: C, 47·7; H, 7·55. $C_{13}H_{24}O_4N_6$ requires C, 47·55; H, 7·35%).

1 : 3 : 4-*Trimethyl*-$\Delta^3$-cyclo*hexenyldimethylcarbinol*.—A solution of methyl 1 : 3 : 4-trimethyl-$\Delta^3$-tetrahydrobenzoate (150 g.) in dry ether (150 c.c.) was added with stirring to the Grignard compound derived from methyl iodide (465 g.), magnesium (80 g.), and dry ether (700 c.c.) at such a rate as to promote and maintain gentle refluxing. After ½ hour's stirring, the product was decomposed with ammonium chloride solution and ice. The carbinol was extracted with ether, washed with brine, dried over sodium sulphate, and freed from solvent. The residue was a rather viscous, yellow oil which proved on distillation to be heterogeneous. The distillate (143 g.) also was heterogeneous (b. p. 101—110°, $n_D^{15·5°}$ 1·4927—1·4877, $d_{4°}^{15·5°}$ 0·9264—0·9249) and could not be resolved into its components by fractionation under an 18-inch vacuum-jacketed column; moreover a portion (b. p. 106—109°) dehydrated by twice treating it with potassium bisulphate (see below) gave a crude hydrocarbon containing an oxygen-containing but non-hydroxylic component.

The remaining (undehydrated) fractions of the crude carbinol were united and a part (50 g.) was dissolved in absolute alcohol (316 c.c.) and refluxed with glacial acetic acid (30 g.) and the Girard reagent " T " (25 g.) on a steam-bath for 45 minutes. The resulting solution (a little reagent was undissolved) was poured into ice-water (1670 g.) containing 18 g. of sodium hydroxide. The product, which changed the colour of bromothymol-blue from blue to yellow, was extracted with ether; the extract was dried over sodium sulphate, and the solvent removed, leaving the non-ketonic component of the crude carbinol. The aqueous mother-liquor was acidified with concentrated hydrochloric acid (167 c.c.), kept overnight, and extracted with ether The extract yielded on evaporation a liquid, from which the *semicarbazone* of 1-acetyl-1 : 3 : 4-trimethyl-$\Delta^3$-*cyclo*hexene was prepared; this crystallised from aqueous alcohol in colourless needles, m. p. 151° (Found: C, 64·1; H, 9·35. $C_{12}H_{21}ON_3$ requires C, 64·5; H, 9·45%).

The non-ketonic portion was submitted to several fractionations at 0·5 mm. pressure (finally under an 18-inch vacuum-jacketed column packed with a spiral of nichrome wire), the progress of fractionation being followed by plotting b. p. and refractive index curves. A reasonably sharp separation into two quite distinct substances was thus made, the highest-boiling fractions (b. p. 105—108°) consisting of practically pure 1 : 3 : 4-*trimethyl*-$\Delta^3$-cyclo*hexenyldimethylcarbinol* (Found: C, 78·95; H, 12·25. $C_{12}H_{22}O$ requires C, 79·05; H, 12·15%), which had $d_{0°}^{17·2°}$ 0·9475, $n_D^{17·2°}$ 1·4956, $[R_L]_D$ 56·20 (calc., 56·47). The lowest-boiling fractions (b. p. 68—71°), after a final redistillation, gave an apparently homogeneous liquid, which had $d_{0°}^{16°}$ 0·8995 and $n_D^{16°}$ 1·4612. This ether-like substance of characteristic odour was mono-olefinic (unsaturation value by hydrogenation, 200·5. Calc., 196·3) and was probably the methyl ether of the carbinol, *viz.*, *methyl* α-1 : 3 : 4-*trimethyl*-$\Delta^3$-cyclo*hexenyl*iso*propyl ether* (Found: C, 79·95, 79·95; H, 12·2, 12·15. $C_{13}H_{24}O$ requires C, 79·5; H, 12·3%).

*Dehydration of* 1 : 3 : 4-*Trimethyl*-$\Delta^3$-cyclo*hexenyldimethylcarbinol*.—The carbinol (12 g.) was refluxed for 45 minutes with finely powdered potassium bisulphate (20 g.). The cooled product was treated with water, and the suspended hydrocarbon taken up in ether. The ethereal solution was washed with sodium carbonate and with water, dried with calcium chloride, and evaporated. The residue was distilled at 0·5 mm. pressure and the bulk of the distillate (9 c.c.) was refluxed with sodium and finally distilled at 761 mm. pressure over sodium, a 6-inch column filled with glass beads being used. Two fractions were collected: (i) b. p. 200—201·5° (0·2 c.c.) and (ii) 202—203° (7 c.c.), leaving a tiny residue. Fraction (ii) was the synthetic dimeride, 1 : 3 : 4-*trimethyl*-1-iso*propenyl*-$\Delta^3$-cyclo*hexene* (Found: C, 87·35; H, 12·4. $C_{12}H_{20}$ requires C, 87·7; H, 12·3%); it had $d_{0°}^{16°}$ 0·8626, $n_D^{16°}$ 1·4823, $[R_L]_D$ 54·42 (calc., 54·45).

This substance behaved (*a*) on hydrogenation, (*b*) towards bromine, and (*c*) towards amyl nitrite and hydrochloric acid in exactly the same way as the above-described acid-formed dimeride, except that no portion of the dibromide of the half-hydrogenated dimeride has yet been obtained in solid form (compare p. 16).

*Addition of Ethyl Crotonate to βγ-Dimethylbutadiene.*—The hydrocarbon (10 c.c.) and the ester were heated together in a sealed tube for 22 hours at 180°. The product on distillation gave largely a colourless ester, b. p. 127—130°/30 mm. (redistilled, b. p. 127—130°/28 mm.), together with some unchanged ester and a clear yellow viscous residue. The first of these was *ethyl* 2 : 4 : 5-*trimethyl*-$\Delta^4$-*tetrahydrobenzoate* (Found: C, 73·2; H, 10·15. $C_{12}H_{20}O_2$ requires C, 73·4; H, 10·25%), which had $n_D^{20°}$ 1·4607, $d_0^{20°}$ 0·9594, $[R_L]_D$ 56·66 (calc., 56·60). 2 : 4 : 5-*Trimethyl*-$\Delta^4$-*tetrahydrobenzanilide*, formed as above from the ester, aniline, and ethylmagnesium bromide, separated in colourless needles, m. p. 162°, from methyl alcohol (Found: C, 79·1; H, 8·6. $C_{16}H_{21}ON$ requires C, 79·0; H, 8·65%). 2 : 4 : 5-*Trimethyl*-$\Delta^4$-*tetrahydrobenzoic acid*, obtained by boiling the ester for 10 minutes with excess of alcoholic potassium hydroxide, formed colourless leaflets, m. p. 137°, from dilute acetic acid (Found: C, 71·3; H, 9·35. $C_{10}H_{16}O_2$ requires C, 71·45; H, 9·6%).

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## 5. *The Hydration of Acetylenes. Part II. Penta-2-yne. Reactivity in Homologous Series.*

By E. L. R. MOWAT and J. C. SMITH.

The hydration of penta-2-yne with 80% sulphuric acid has been studied by estimation of the amounts of methyl propyl and of diethyl ketone produced. The results along with those of the hydration of $\Delta^9$-undecynoic acid show that in the reaction

$$2CH_3\cdot C\vdots CR + 2H_2O \longrightarrow CH_3\cdot CH_2\cdot COR + CH_3\cdot CO\cdot CH_2R$$

the acetylenes display increasing reactivity with increasing length of alkyl chain (Homologous Series Reactivity, Type III; Abraham, Mowat, and Smith, J., 1937, 948). This is due to the increase of negativity of carbon attached to alkyl (general effect), and the steric or orientation effect is considered to act equally on both the carbon atoms.

IN Part I (Sherrill and Smith, J., 1937, 1501) the hydration of $\Delta^9$-undecynoic acid ($CH_3\cdot C\vdots C\cdot[CH_2]_7\cdot CO_2H$) with sulphuric acid was shown to give 59% of 9-keto- and 41% of 10-keto-undecoic acid. It was hoped to obtain a comparable analysis of the hydration products of penta-2-yne, but none of the methods available gave accurate results and the hydration was accompanied by some polymerisation.

$$CH_3\cdot C\vdots C\cdot C_2H_5 + H_2SO_4,H_2O \longrightarrow CH_3\cdot CH_2\cdot CO\cdot C_2H_5 \quad (52\%)$$
$$CH_3\cdot C\vdots C\cdot[CH_2]_7\cdot CO_2H + H_2SO_4,H_2O \longrightarrow CH_3\cdot CH_2\cdot CO\cdot[CH_2]_7\cdot CO_2H \quad (59\%)^1$$
$$CH_3\cdot CH\vdots CH\cdot C_2H_5 + HBr \longrightarrow CH_3\cdot CH_2\cdot CHBr\cdot C_2H_5 \quad (53\%)^2$$
$$CH_3\cdot CH\vdots CH\cdot[CH_2]_7\cdot CO_2H + HBr \longrightarrow CH_3\cdot CH_2\cdot CHBr\cdot[CH_2]_7\cdot CO_2H \quad (50\%)^3.$$

[1] Part I, *loc. cit.* [2] Lauer and Stodola, *J. Amer. Chem. Soc.*, 1934, **56**, 1215.* [3] Abraham, Mowat, and Smith, *loc. cit.*

The first two results above show that in the hydration of a series of acetylenes, $CH_3\cdot C\vdots CR$, with sulphuric acid the relative reactivity of C attached to alkyl *increases* with increasing length of the alkyl chain; this is an example of homologous series reactivity, type III (Abraham, Mowat, and Smith, *loc. cit.*).

Consideration of series in which there is a large fall in reactivity in passing from $CH_3X$ to $C_2H_5X$ . . . $C_4H_9X$ as in the *n*-alkyl iodides when reacting with sodium phenoxide (Segaller, J., 1913, **103**, 1154) shows that these are cases in which both a general effect and a steric or orientation factor should exist. Thus in the formation of phenol ethers ($R\cdot CH_2I$ + NaOPh) the tendency of the methylene group to attach itself to the oxygen

* The value 79% of 3-bromopentane found by Lucas and Moyse (*ibid.*, 1925, **47**, 1459) has now been withdrawn (Lucas and Prater, *ibid.*, 1937, **59**, 1682; see also Sherrill and Matlack, *ibid.*, p. 2134).

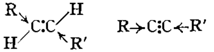
atom should be lessened by the general effect of the larger *n*-alkyl group (which will make the $\alpha$-methylene group more negative); but much more important should be the steric factor: the probability that the $\alpha$-methylene group will be in a suitable position for reaction to occur will be greatly diminished as R changes from hydrogen to *n*-propyl. That the differences in charge between the carbon atoms attached to iodine are small is shown by the dipole moments of vapours of alkyl iodides (Groves and Sugden, J., 1937, 158):

| | | | | |
|---|---|---|---|---|
| R = | H. | Me. | Et. | *n*-Pr. |
| $\mu$ = | 1·64 | 1·87 | 2·01 | 2·08 e.s.u. $\times 10^{-18}$ |

(The differences are smaller for a series of bromides or chlorides.)

Owing to the polarisability of triple bonds it is possible for the alkyl groups in acetylenes to induce by their (opposed) general effects sufficient polarity to influence the composition of the product of hydration with sulphuric acid. Allowing for errors of $\pm 3\%$ in both the results quoted, it seems that in the olefins the polarisation is insufficient to influence the addition of hydrogen bromide; there is no information as to whether it can affect the hydration with sulphuric acid. In those cases where the proportions of two addition products are being measured and both alkyl groups are in the same molecule it is obvious that the *orientation factor* need not be considered: it may affect the reactivity of the molecule as a whole, but should not affect the *relative* reactivity of the unsaturated carbon atoms.

A factor which may be of importance is the angle through which the effects are directed towards the double or triple bond. If it is considered that in the olefins the polarisation



is altered by this angle, the effects should be 0·58 $\left(= \cos \frac{109° 28'}{2}\right)$ of those in the acetylenes.

## Experimental.

*Penta-2-yne.*—A solution of $\beta$-amylene (250 g., Messrs. British Drug Houses Ltd.) in carbon disulphide (300 c.c.) was stirred in a freezing mixture while bromine (570 g.) in carbon disulphide (400 c.c.) was added. After the solvent had been removed the dibromo-compound was distilled at 90°/14 mm. (yield, 750 g.). Powdered potassium hydroxide (300 g.) and alcohol (400 c.c. of 98%) were stirred in a 3-neck flask heated in an oil-bath until most of the potash was in solution. The flask was provided with a mercury seal, a dropping-funnel, and a condenser kept at 40° to return alcohol. Vapour which passed this condenser was led to a second condenser kept at 0°.

A vigorous reaction was kept going by dropping in dibromopentane (200 g.) and it was possible by stirring to obtain a regular distillation of pentyne. When all the bromo-compound had been added, the temperature of the oil-bath was raised and alcohol allowed to distil until the total had reached 150 c.c. The residue in the reaction flask was largely diluted with water, and the bromopentene layer separated for heating with alcoholic potassium hydroxide in sealed tubes (Faworsky, *J. pr. Chem.*, 1888, **37**, 382). Fractionation of the pentyne distillate gave 35—45 g., b. p. 40—60°, containing apparently more penta-1-yne than penta-2-yne.

*Conversion into Penta-2-yne.*—The crude pentyne (15 c.c.) was heated with concentrated alcoholic potassium hydroxide solution (6 c.c.) in a sealed tube for 20 hours at 200°. The products from several experiments were well washed with water to remove alcohol and dried. Fractionation with a Young column easily separated penta-1-yne from penta-2-yne. Fraction (i), b. p. 36—55·0° (15 g.), and fraction (ii), 55·0—55·5° (14 g.), gave precipitates with alcoholic silver nitrate; fractions (iii), 55·5—55·6° (9·5 g.), (iv) main fraction, 55·6°/760 mm. (15 g.), and (v), 55·6—56·0° (6·0 g.), gave no precipitate with silver nitrate. There was a residue of polymerised material (30—40 g.). Fractions b. p. 55—55·5° were used for preliminary experiments and fractions b. p. < 55° were reheated with alcoholic potassium hydroxide.

*Diethyl Ketone.*—The commercial product was distilled; the main fraction (b. p. 101·8—102·2°) yielded a semicarbazone, m. p. 137—138°, raised by two crystallisations from methyl alcohol to 139—140°. Dilthey (*Ber.*, 1901, **34**, 2122) gives m. p. 139°. A specimen of diethyl

ketone from propionitrile and ethylmagnesium bromide boiled at 101—102° and yielded a semicarbazone of m. p. 139°. The *p*-nitrophenylhydrazone melted at 140—141° (van Ekenstein and Blanksma, *Rec. trav. chim.*, 1903, **22**, 435, give m. p. 141°).

*Methyl Propyl Ketone.*—A sample boiling constantly at 102·0° gave a crude semicarbazone, m. p. 96°, which after four crystallisations from methyl alcohol gave a small yield of plates, m. p. 113°. Bouveault and Bongert (*Bull. Soc. chim.*, 1902, **27**, 1083) give m. p. 112°. Benzene was of little use for the purification and it was possible that the crude semicarbazone contained some of the yet unknown geometrical isomeride. A specimen of the ketone from ethyl ethylacetoacetate also gave a crude semicarbazone, m. p. 96°, and after recrystallisation, 111°. The crude *p*-nitrophenylhydrazone melted at 108—110° and after many crystallisations from alcohol, alcohol–pyridine, and alcohol–acetic acid it melted at 116°. Fischer and Tropsch (*Ber.*, 1923, **56**, 2433) give m. p. 116—117°.

*Mixtures of the Semicarbazones of Pentan-2- and -3-one.*—Preliminary determinations showed that the system was of the eutectic type and that mixtures containing more than 70% of the semicarbazone of pentan-3-one melted with slight decomposition. The curve from the following m. p.'s (thermometer in the liquid) was used in the analysis of mixtures :

| | | | | | |
|---|---|---|---|---|---|
| Pentan-3-onesemicarbazone, mols. % ... | 62·7 | 60·0 | 55·0 | 50·0 | 47·0 |
| M. p. ...... | 116·1° | 113·5° | 109·0° | 104·3° | 101·4° |

*Mixtures of the* p-*Nitrophenylhydrazones of Pentan-2- and -3-one.*—The curve was drawn from the following points (thermometer in the liquid) :

| | | | | |
|---|---|---|---|---|
| Pentan-3-one-*p*-nitrophenylhydrazone, mols. % ...... | 64·3 | 58·1 | 50·0 | 43·4 |
| M. p. ...... | 122·1° | 118·1° | 112·2° | 106·5° |

*Hydration of Penta-2-yne.*—The following method was finally adopted, as it gave high yields and only a little polymerisation occurred. Sulphuric acid (16 c.c. of 80%) was cooled to 0° in a 50 c.c. stoppered flask. Penta-2-yne (4·0 c.c., 2·9 g.), cooled to 0°, was added in one portion, and the flask shaken vigorously while cooled with ice-water. After 8 minutes the smell of acetylene was replaced by the pleasant smell of ketones, and after a total of 10 minutes the mixture was poured on ice. The ketones were carefully extracted (four extractions), a total of 20—30 c.c. of purified light petroleum (b. p. 50—60°, freed from olefins) being used (extraction with ether led to losses, benzene formed emulsions, and chloroform reacted with the ketones). In some experiments the extract was distilled at about 250 mm. pressure from a small flask, and the vapour condensed in receivers cooled in a freezing mixture. Traces of high-boiling liquid were left in the flask.

*Analysis of the Hydration Products.*—Physical methods of analysis such as the refractive index method were ruled out by the similarity of physical properties of the ketones.

Pringsheim and Gorgas (*Ber.*, 1924, **57**, 1361) have recommended measurement of the rate of oxime formation, but this did not appear to be a sufficiently accurate process. Although methyl propyl ketone reacted enormously faster than diethyl ketone with sodium bisulphite solution, the reaction was incomplete even in presence of a large excess of bisulphite. Precipitation of the 2 : 4-dinitrophenylhydrazones gave products slightly contaminated with the reagent. Finally the semicarbazones and *p*-nitrophenylhydrazones were used and corrections were applied for the greater solubility of the methyl propyl ketone derivatives.

*Analysis as Semicarbazones.*—The extract of the products of hydration was shaken for 48 hours in a stoppered bottle with semicarbazide hydrochloride (6·0 g.) and potassium acetate (7·5 g.) in water (10 c.c.). The liquid was then filtered into a separating funnel. The aqueous layer was extracted with light petroleum and then all the petroleum liquors were evaporated. In order to remove semicarbazide the total solid residues were ground with water (10 c.c.), collected, and dried in a vacuum. An alternative method of washing was to dissolve the semicarbazones in chloroform (18 c.c.) and to extract the solution rapidly twice with water (10 c.c. each time). Experiments carried out with a 50/50 mixture of the ketones showed that the first method of isolation and washing caused an average rise of 2·6° in the m. p., and the second method a rise of 1·2°. The semicarbazones were slowly hydrolysed by water.

*Hydration A* gave 4·94 g. (81% yield) of washed semicarbazones (Found: N, 29·7. Calc., 29·4%), m. p. 106·5° (corrected for solubility, 103·9°), indicating 49·5% of diethyl ketone.

*Hydration B* (the extract of the ketones was distilled) gave 4·7 g. (78% yield) of semicarbazones (Found: N, 29·6), m. p. 108° (corrected 106·8°), indicating 52·5% of diethyl ketone.

*Analysis as* p-*Nitrophenylhydrazones.*—Tests were made on a solution containing 55 parts of diethyl ketone to 45 parts of methyl propyl ketone (4 g. of mixture in 25 c.c. of light

petroleum). The solution of the ketones (4·0 c.c.) was added to a clear solution of *p*-nitrophenylhydrazine (1·7 g.) in acetic acid (6 c.c.) and water (4 c.c.) and the mixture was left for 3 days with frequent periods of shaking on a machine. Water (10 c.c.) was then added, and the mixture left for 1 hour. After the light petroleum had been removed carefully in a vacuum, the liquid was filtered, and the solid washed with acetic acid (twice with 5 c.c. of 20%) and then with water (5 c.c.). It was dried in a vacuum over potassium hydroxide. From the melting point, 118° (119° for the product of a second experiment) a composition of 59% of diethyl ketone was indicated, so a correction of − 4% had to be applied. (The yields were 1·9 and 2·05 g., 78 and 86% respectively.) A similar test on a 50/50 mixture of the ketones in light petroleum gave a product, m. p. 116°, indicating a correction of − 5%.

Hydrations were carried out as in experiments A and B, the product being extracted with light petroleum and the volume made up to 25 c.c. For analysis 4—5 c.c. of the solution were shaken with *p*-nitrophenylhydrazine as described above.

*Hydration C.* 4·0 C.c. of extract yielded 1·5 g. of solid (Found: N, 19·2. Calc., 19·0%). The m. p. 115·2° (54% of the diethyl ketone derivative) indicated a corrected value of 50% of diethyl ketone.

*Hydration D.* The extract of the ketones was distilled before the volume was made up to 25 c.c. From 4·5 c.c. of this extract 1·6 g. of *p*-nitrophenylhydrazones were obtained (Found: N, 19·2%). The m. p. 116·5° (56·5%) indicated 52% of diethyl ketone.

*Hydration E.* The sulphuric acid solution of the ketones was poured on ice, the mixture neutralised with 30% sodium hydroxide solution, and steam passed. The ketones were carefully extracted from the distillate (60 c.c.) with light petroleum (25 c.c.). 4·0 C.c. of this extract yielded 1·4 g. of *p*-nitrophenylhydrazones, m. p. 118° (58%), indicating 54% of diethyl ketone.

| Hydration. | Method of analysis. | Diethyl ketone, mols. %. | Hydration. | Method of analysis. | Diethyl ketone, mols. %. |
|---|---|---|---|---|---|
| A | Semicarbazones | 49·5 | D | *p*-Nitrophenylhydrazones | 52 |
| B | ,, | 52·5 | E | ,, ,, | 54 |
| C | *p*-Nitrophenylhydrazones | 50 | Mean | | 52 |

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## 6. *Chemotherapeutic Studies in the Acridine Series. Part III. 4-Amino-, 1 : 3-, 1 : 7-, and 3 : 6-Diaminoacridines.*

By Adrien Albert and Wilfred H. Linnell.

The above acridine derivatives have been prepared in completion of an exploration of the relationship between the chemistry and the antiseptic activity of the simpler aminoacridines. 1 : 3-Diaminoacridone is easily oxidised in air, but 1 : 3-diaminoacridine is stable. The presence of 1- and 4-amino-substituents leads always to compounds which are non-fluorescent in alcoholic solution, even when the corresponding substances without these groups fluoresce actively. Furthermore the preliminary bacteriological tests indicate that all the compounds containing a 1-amino-substituent are without antiseptic effect, whereas the 4 (as well as the 5, 3, and 2)-amino-group greatly increases the antiseptic activity of the acridine molecule.

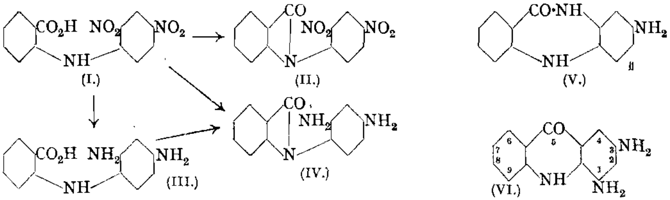
A substance described in 1885 as 1 : 3-diaminoacridone has now been found to be a diaminodiphenylaminecarboxylic acid lactam.

2-Chloro-5-nitrobenzoic acid was condensed with *m*-nitroaniline to give 4 : 3′-*dinitrodiphenylamine*-2-*carboxylic acid*, and 2-chlorobenzoic acid and 3 : 5-dinitroaniline similarly gave 3′ : 5′-*dinitrodiphenylamine*-2-*carboxylic acid*. The latter on ring closure with phosphorus oxychloride, followed by acid hydrolysis, yielded 2 : 4-*dinitroacridone*. When 4 : 3′-dinitrodiphenylamine-2-carboxylic acid was treated with phosphorus oxychloride and the usual precautions were taken to avoid hydrolysis (see Part I, J., 1936, 88), a 2% yield only of *meso*chlorodinitroacridines was obtained, from which 5-*chloro*-2 : 7-*dinitroacridine* was isolated by fractional crystallisation; the bulk of the condensation product was a mixture of 2 : 7 (*i.e.*, 3 : 8)- and (mainly) 3 : 6-dinitroacridones, since on further treatments with phosphorus oxychloride small additional amounts of 5-chloro-2 : 7-

dinitroacridine could be obtained, and complete reduction led to 3 : 6-*diaminoacridine*, a substance distinctly different from 2 : 7-diaminoacridine (Part II, J., 1936, 1614) in properties. The failure of the above dinitroacridones to yield *meso*chloro-compounds to any extent is consonant with our experience of acridones containing an odd-numbered nitro-group. 1 : 7-Dinitroacridone on acid reduction gave 1 : 7-*diaminoacridone*, but 2 : 4-dinitroacridone gave a product which was oxidised in the air so rapidly that it could not be obtained analytically pure.

1 : 7-Diaminoacridone and 4-aminoacridone (Lehmstedt, *Ber.*, 1937, **70**, 838) on reduction with sodium amalgam gave respectively 1 : 7-*diaminoacridine* and 4-*aminoacridine*. As 1 : 3-diaminoacridone (Drozdov, *J. Gen. Chem. U.S.S.R.*, 1934, **4**, 1) when similarly treated failed to give the corresponding acridine, 2-aminobenzaldehyde and 2 : 4-dinitrobromobenzene were condensed together to give 1 : 3-dinitroacridine, which on acid reduction furnished the required 1 : 3-*diaminoacridine*.

All known aminoacridones fluoresce in alcoholic solution, but the 1- and 4-amino-substituted acridines produced in this work are devoid of such fluorescence. Contrary to a published statement (Ullmann, *Ber.*, 1907, **40**, 2522) 1-aminoacridine does not fluoresce in alcoholic solution, nor do its salts fluoresce in water (Lehmstedt, private comm.).



*Reduction of* 2′ : 4′-*Dinitrodiphenylamine-2-carboxylic Acid* (I).—By vigorous reduction of this acid with tin and alcoholic hydrogen chloride, Jourdan (*Ber.*, 1885, **18**, 1444) obtained, in place of the expected diamino-acid (III), a yellow compound which he regarded as 1 : 3-diaminoacridone (" Diamidohydroacridinketon ") (VI). However, when stannous chloride in cold acetic acid was used, 2′ : 4′-*diaminodiphenylamine-2-carboxylic acid monohydrochloride* was formed instead. When the stannichloride of this substance was heated with tin and hydrochloric acid, " Jourdan's compound " was obtained, and this was hydrolysed by methyl-alcoholic potash to the parent amino-acid (III). As 1 : 3-diaminoacridone, obtained by the reduction of 1 : 3-dinitroacridone (Drozdov, *loc. cit.*), differs in colour, solubility in alkali, melting point, and air-stability from " Jourdan's compound," and displays a fluorescence which the latter lacks, it is evident that the latter is an anhydro-compound of the type (IV) or (V). Since Drozdov (*loc. cit.*), by the action of phosphorus oxychloride on the sodium salt of (I), obtained the 1 : 2-lactam (II), it seems likely in the present case that stannous chloride functioned similarly as a condensing agent to give (IV) (cf. also Clemo, Perkin, and Robinson, J., 1924, **125**, 1779). On gentle acetylation a diacetyl compound, 2′ : 4′-*bisacetamidodiphenylamine-2-carboxylic acid* 1 : 2-*lactam*, was obtained, and this re-formed " Jourdan's compound " on acid hydrolysis. " 7-Chloro-1 : 3-diaminoacridone " (Jourdan, *loc. cit.*) would appear likewise to be a lactam.

The pharmacological testing of these compounds was carried out by Dr. F. J. Dyer in the Pharmacological Laboratories of this College (*Quart. J. Pharm. Pharmacol.*, 1936, No. 4), and the bacteriological testing by Dr. L. P. Garrod of St. Bartholomew's Hospital (in the press). Preliminary biological tests have revealed that antiseptic activity and toxicity are not parallel in this series; for example, 2 : 7-diaminoacridine is comparable with proflavine in bacteriostatic properties but is 2·5 times less toxic, and 10 times less toxic than acriflavine; but 2-chloro-5-aminoacridine is twice as bacteriostatic as proflavine and twice as toxic. Whenever a 1-amino-group is introduced into an acridine compound, the antiseptic properties are completely destroyed.

## Experimental.

*Diphenylaminecarboxylic Acids.*—Sodium *o*-chlorobenzoate (3 g.), 3 : 5-dinitroaniline (3 g.), precipitated copper (0·1 g.), sodium carbonate (0·45 g., ½ mol.), and 4-methyl*cyclo*hexanol (20 ml.) were refluxed for 4 hours, and the 3′ : *5′-dinitrodiphenylamine-2-carboxylic acid* purified similarly to its isomeride (Part I). Yield, 22% of brownish-orange crystals, m. p. 263° (corr.), only slightly soluble in most solvents, soluble approx. 1 in 22 of boiling glacial acetic acid, but 90% acetic acid is more suitable for recrystallisation (Found: C, 51·85; H, 3·1; N, 13·4. $C_{13}H_9O_6N_3$ requires C, 51·5; H, 3·0; N, 13·9%). The colourless solution in sulphuric acid was turned deep orange by a trace of a nitrate. The orange-brown sodium salt was soluble in hot water and readily salted out with sodium carbonate.

Sodium 2-chloro-5-nitrobenzoate (4·5 g.), *m*-nitroaniline (4·2 g., 1½ mols.), precipitated copper (0·1 g.) and nitrobenzene (20 ml.) were refluxed for 1½ hours, and the 4 : 3′-*dinitrodiphenylamine-2-carboxylic acid* purified as above. Yield, 20% of pale brownish-yellow crystals, m. p. 229° (corr.), only slightly soluble in most solvents and best crystallised from 100 parts of boiling glacial acetic acid (Found: C, 51·7; H, 3·1; N, 13·9%). The yellow solution in sulphuric acid was unchanged by the addition of a trace of a nitrate. The bright orange sodium salt was readily salted out by sodium carbonate.

2′ : 4′-Dinitrodiphenylamine-2-carboxylic acid (2 g.) and anhydrous stannous chloride reagent (120 ml.; Part II) were left for 2 days in the cold, the lumps being broken as formed. An aqueous solution of the stannichloride was freed from tin with hydrogen sulphide and treated with sodium acetate, giving a white crystalline precipitate, soluble in sodium hydroxide solution, of 2′ : 4′-*diaminodiphenylamine-2-carboxylic acid hydrochloride* in 60% yield, m. p. 252° (corr.) (with effervescence and sublimation) (Found: C, 55·9; H, 5·2; N, 14·8; Cl, 12·4. $C_{13}H_{13}O_2N_3$,HCl requires C, 55·8; H, 5·0; N, 15·0; Cl, 12·7%). When heated for 15 hours at 140° in the air, it became in turn lilac, violet, and brown, but the m. p. remained unchanged. It was soluble in hot water, and was partly deposited on cooling, more completely on addition of sodium chloride. The free acid could not be precipitated by the use of buffers (internal salt formation ?). The hydrochloride was soluble in most organic solvents without temperature gradient and was best recrystallised by solution in 85% alcohol (1—30) and addition of twice that volume of benzene. It gave a red coloration with nitrous acid, intensified by alkaline β-naphthol, although not by alkali alone. Ferric chloride gave a scarlet colour, and the phenanthraquinone test for an *o*-diamine was also given. The colourless solution in sulphuric acid was turned deep yellow by a trace of a nitrate. Instead of stannous chloride, ferrous chloride and boiling aqueous ammonia may be used as a reducing agent in the preparation of this substance.

*Jourdan's Compound.*—A mixture of 2′ : 4′-diaminodiphenylamine-2-carboxylic acid stannichloride (5 g.), alcohol saturated with hydrogen chloride (70 ml.), and excess of tin was refluxed for an hour and evaporated to half-volume. The product was poured into water and treated with excess of sodium hydroxide. The precipitate was taken up in hot dilute hydrochloric acid; the solution, on cooling, deposited the hydrochloride of " Jourdan's compound " in 40% yield. Ammonia liberated the free base in golden spangles having the properties described by Jourdan, as well as the following, hitherto unrecorded (Found: N, 18·4; *M*, in camphor, 244. Calc. for $C_{13}H_{11}ON_3$: N, 18·6%; *M*, 225): The substance did not fluoresce, neither did it give a precipitate in alcohol with mercuric chloride. 50% Sulphuric acid and a trace of a dichromate gave a deep brown solution, the odour of quinone becoming perceptible on warming. On diazotisation an orange solution was obtained, which became deep red on addition of alkaline β-naphthol.

The above compound (0·2 g.) and N-90% methyl-alcoholic potash (10 ml.) were refluxed for 1½ hours, and the alcohol then distilled. A filtered aqueous solution of the residue on treatment with hydrochloric acid and sodium acetate gave 2′ : 4′-diaminodiphenylamine-2-carboxylic acid hydrochloride in 50% yield, m. p. (after crystallisation from alcohol–benzene) and mixed m. p. 252°. " Jourdan's compound " (0·5 g.) and acetic anhydride (0·5 g.) were heated for 15 minutes on the water-bath, and the white precipitate of 2′ : 4′-*bisacetamidodiphenylamine-2-carboxylic acid* 1 : 2-*lactam* filtered off. Yield 92%, m. p. 307° (corr.) (Found: C, 65·8; H, 4·8; N, 13·3. $C_{15}H_{15}O_3N_3$ requires C, 66·0; H, 4·9; N, 13·6%). It was soluble in 30% alcohol (approx. 1 in 75, boiling, with 84% recovery on cooling) and in stronger alcohol without temperature gradient, almost insoluble in toluene, chloroform, and water, was not diazotisable, and gave no colour with ferric chloride. When it was warmed with sulphuric acid in alcohol, " Jourdan's compound " was re-formed.

*Ring Closure and Formation of* meso*Chloro-compounds.*—A mixture of 3′ : 5′-dinitrodiphenylamine-2-carboxylic acid (0·5 g.) and phosphorus oxychloride (5 ml.) was refluxed for an hour and poured into water. The precipitate was boiled with 5% hydrochloric acid for 15 minutes, dried, and dissolved in N/5-50% alcoholic potash, and the deep red solution treated with acid, giving 2 : 4-*dinitroacridone* in 94% yield. The product was dissolved in pyridine, and boiling benzene (3 vols.) gradually added; on cooling, golden-brown infusible needles were obtained, almost insoluble in acetic acid and other common solvents, but somewhat soluble in hot 20% aqueous sodium hydroxide with a dark brown colour (Found : C, 54·9; H, 2·6; N, 14·4. $C_{13}H_7O_5N_3$ requires C, 54·7; H, 2·5; N, 14·7%).

1 : 7-Dinitroacridone was produced in 61% yield (calculated on the bromonitrobenzene) by nitration of 1-nitroacridone, obtainable in excellent yield by ring closure of the corresponding nitrodiphenylamine-2-carboxylic acid (Ullmann, *Annalen*, 1907, **355**, 327).

5 : 4′-Dinitrodiphenylamine-2-carboxylic acid (2·7 g.) and phosphorus oxychloride (16 ml.) were refluxed for 8 hours, most of the solvent recovered, and the product treated with ice and ammonia. On extraction with chloroform and recrystallisation of the residue, remaining after evaporation, from benzene a 20% yield of yellow 5-*chloro*-2 : 7-*dinitroacridine* was obtained, m. p. 233° (corr.) (Found : N, 14·1. $C_{13}H_6O_4N_3Cl$ requires N, 13·85%).

Neither 2′ : 4′-dinitrodiphenylamine-2-carboxylic acid (I) nor 1 : 3-dinitroacridone furnished a *meso*chloro-compound.

2-Aminobenzaldehyde (5·2 g.), 2 : 4-dinitrobromobenzene (10·8 g.; 1 mol.), precipitated copper (0·5 g.), sodium carbonate (2·3 g.), and nitrobenzene (40 ml.) were heated in an oil-bath at 215° for 3 hours. After steam-distillation and filtration, the residue was heated with sulphuric acid (20 ml.) on the water-bath for an hour, the product poured into water (10 vols.), the solution filtered at the b. p., and aqueous ammonia added to the filtrate. The precipitated 1 : 3-dinitroacridine crystallised from pyridine in brownish-orange needles, m. p. 284° (corr.), only slightly soluble in cold dilute acids (yield, 30%).

*Acid Reductions.*—The reduction of 1 : 3-dinitroacridone with anhydrous stannous chloride reagent (Part II), followed by decomposition of the stannichloride with ammonia and extraction of the precipitate with alcohol, produced 1 : 3-diaminoacridone (Drozdov, *loc. cit.*), for which the following properties may now be recorded : it fluoresces bright green in alcoholic solution, is decomposed to a blue product by hydrogen sulphide, and is very readily oxidised in the air to a black insoluble product. Neither this product nor 1 : 3-dinitroacridone, when reduced with sodium amalgam by the methods described in Part II, gave any 1 : 3-diaminoacridine, which was, however, prepared in 75% yield by the action of anhydrous stannous chloride reagent on 1 : 3-dinitroacridine. The stannichloride was decomposed with excess of sodium hydroxide and the precipitate formed was extracted with alcohol. After recrystallisation from alcohol, 1 : 3-*diaminoacridine* formed air-stable, orange, feathery crystals, m. p. 225° (sealed tube, corr., decomp.), slightly soluble in boiling water and chloroform, insoluble in sodium hydroxide solution (Found : C, 74·7; H, 5·2; N, 19·5. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3; N, 20·1%). Neither the base nor its salts fluoresce in alcohol or in water. The purple hydrochloride and the sulphate are soluble in water and the solutions are decolourised by nitrous acid, becoming orange on addition of sodium hydroxide or alkaline β-naphthol.

1 : 7-Dinitroacridone on reduction with the stannous chloride reagent gave a precipitate of the stannichloride, which was treated with ice and sodium hydroxide, more than a slight excess being avoided. The precipitate was dried at 120°, and the base extracted in dilute hydrochloric acid and reprecipitated with sodium hydroxide (slight excess), a 50% yield of 1 : 7-*diaminoacridone* being obtained; this, on recrystallisation from boiling water (1 in 2,500; 60% recovery), gave lemon-yellow needles, charring at 330°, only slightly soluble in alcohol, very soluble in alcoholic potash, and moderately in 4% aqueous sodium hydroxide (Found : C, 69·2; H, 4·7; N, 17·95. $C_{13}H_{11}ON_3$ requires C, 69·3; H, 4·9; N, 18·6%). The intense yellow-green fluorescence of an alcoholic solution was destroyed by acid; and there was no fluorescence of the base in acetic acid or of the hydrochloride in water. The diazotised solution was pale orange, becoming deep red with alkaline β-naphthol.

Reduction in the same way of the mixture of 2 : 7- and 3 : 6-dinitroacridones (see p. 22) led to a mixture of the aminoacridones, which was reduced to the corresponding diaminoacridines.

*Alkaline Reductions.*—4-Aminoacridone hydrochloride (0·5 g.) was reduced with sodium amalgam, and the product oxidised with ferric chloride (cf. 2 : 6-diaminoacridone; Part I). When the oxidised solution was cooled, the sodium chloride present precipitated 4-*amino-acridine* as the hydrochloride. The base was set free and crystallised from 33% alcohol, giving

a 71% yield of brownish-orange needles, m. p. 181° (corr.; sealed tube; bath at 160°). It was *very soluble in alcohol and chloroform* without temperature gradient, but could be re-crystallised from water (Found for material dried in air at 110°: loss in a vacuum at 120°, 17·0. $C_{13}H_{10}N_2,2H_2O$ requires $H_2O$, 16·0%. Found for material dried in a vacuum at 120°: C, 80·3; H, 5·0. $C_{13}H_{10}N_2$ requires C, 80·4; H, 5·2). Neither the base nor its salts, which were violet, fluoresced in water or organic solvents, but a bright yellow-green fluorescence was shown in concentrated sulphuric acid.

1 : 7-Diaminoacridone, reduced as above, but not treated with acid or ferric chloride, gave a 60% yield of 1 : 7-*diaminoacridine*, which was recrystallised (1 in 2500) from boiling water, giving orange needles, m. p. 126° (corr.; sealed tube), very soluble in alcohol and pyridine, and slightly soluble in chloroform and benzene, all without temperature gradients, but insoluble in alkali. The solubility in boiling water was approx. 1 in 1,000, but more dilute solutions crystallised better (Found: C, 74·1; H, 5·3; N, 19·7. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3; N, 20·1%). Neither the base nor its salts gave any fluorescence in alcohol or water, but the base fluoresced yellow-green in concentrated sulphuric acid. The violet hydrochloride and sulphate were readily soluble in water and on diazotisation gave colourless solutions which became bright red with alkaline β-naphthol. In 50% sulphuric acid a trace of potassium dichromate produced a light brown coloration, whereas 1-aminoacridine gave a violet colour.

The mixture of 2 : 7 and (mainly) 3 : 6-diaminoacridones (*v.s.*) was reduced with sodium amalgam as above, and the product treated with ferric chloride. The resultant mixture was treated with sodium hydroxide, and the precipitate extracted with alcohol. On evaporation of the solvent, solution of the residue in dilute hydrochloric acid, and addition of 10% of sulphuric acid, the sulphate of 3 : 6-*diaminoacridine* was slowly deposited. The base was liberated and recrystallised from 100 parts of alcohol until the solution no longer fluoresced; yellow-brown needles, m. p. 322° (sealed tube; not sharp), were then obtained, which were slightly soluble in boiling water and benzene and very soluble in pyridine. The purple salts were very soluble in water and far less readily salted-out than those of other aminoacridines (Found: C, 74·9; H, 5·2; N, 19·6%). Neither the base nor its salts exhibited fluorescence in water or alcohol. From the mother-liquor a small quantity of 2 : 7-diaminoacridine, m. p. 355° (Found: N, 19·7), and showing a bright green fluorescence in alcohol, was obtained.

A gift of *o*-chlorobenzoic acid from Imperial Chemical Industries (British Dyestuffs Corporation, Blackley) is gratefully acknowledged.

College of the Pharmaceutical Society (University of London), London, W.C. 1. [*Received, November 19th*, 1937.]

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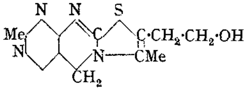
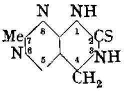
# 7. *Aneurin. Part IX. A New Synthesis of Thiochrome. Note on the Synthesis of Aneurin.*

By F. Bergel and A. R. Todd.

A synthesis of thiochrome from 2-thio-7-methyl-1 : 2 : 3 : 4-tetrahydro-1 : 3 : 6 : 8-benztetrazine and methyl α-chloro-γ-acetoxypropyl ketone is described. *O*-Acetyl-aneurin is shown to be an intermediate product in the synthesis of aneurin described in Part VII (J., 1937, 364). The existence of a low-melting modification of aneurin chloride hydrochloride is confirmed.

The structure of thiochrome (I), the blue-fluorescent oxidation product of aneurin (vitamin $B_1$), has been established by its synthesis from 4-chloro-5-chloromethyl-2-methylpyrimidine and 2-amino-4-methyl-5-β-hydroxyethylthiazole (Todd, Bergel, Fraenkel-Conrat, and Jacob, J., 1936, 1601). This synthesis was, however, unsatisfactory as a practical method for the preparation of the pigment. As larger quantities of thiochrome were required for various purposes, we endeavoured to synthesise it by adapting the procedure used in the synthesis of 3-methylthiazolobenzimidazole (Todd, Bergel, and Karimullah, *Ber.*, 1936, 69, 217). 2-Thio-7-methyl-1 : 2 : 3 : 4-tetrahydro-1 : 3 : 6 : 8-benztetrazine (II) was heated with methyl α-chloro-γ-acetoxypropyl ketone either alone or better in presence of glacial acetic acid; a product was obtained identical with thiochrome prepared from aneurin,

he initially formed acetyl derivative being hydrolysed during the process of working up. 'he yield in this synthesis was again disappointing; further attempts to improve the yield re not contemplated, as the ready accessibility of synthetic aneurin makes the preparation f thiochrome from it an economical process, the yield being 70—80%.

(I.)   (II.)

The preparation of 8-thiopurines by heating 4 : 5-diaminopyrimidines with thiourea Gabriel, *Ber.*, 1901, **34**, 1254) is a satisfactory process, but fusion of 4-amino-5-amino-ıethyl-2-methylpyrimidine with thiourea gave a very small yield of the benztetrazine erivative (II). Condensation of the hydrochloride of 4-amino-5-aminomethyl-2-methyl-yrimidine with potassium thiocyanate, and heating of the substituted thiourea so formed, ave (II) in a yield of 45%. It seems from these results that the benztetrazine ring ystem is much less readily formed than the purine nucleus.

*Note on the Synthesis of Aneurin.*—In Part VII (J., 1937, 364) we described a synthesis f aneurin in which 4-amino-5-thioformamidomethyl-2-methylpyrimidine was condensed ith methyl $\alpha$-chloro-$\gamma$-acetoxypropyl ketone. The crude product yielded the vitamin hloride after several recrystallisations from alcohol containing hydrogen chloride. At ome stage in this process the acetyl group originally present in the chloro-ketone must ave been removed. A probable explanation seemed that it was eliminated by hydrolysis uring the crystallisation process. In support of this view we have isolated from the rude reaction mixture O-*acetylaneurin chloride hydrochloride.* This substance is readily ydrolysed by acids, and yields a crystalline, sparingly soluble picrate, m. p. 176°. The esidual material after removal of the *O*-acetylaneurin yielded, on being worked up as escribed in Part VII (*loc. cit.*), aneurin chloride hydrochloride. When absolute alcohol as used in the crystallisation processes the vitamin chloride had m. p. 236—237°, un-hanged by further recrystallisation from the same solvent. On recrystallisation from 90% lcohol or by seeding with the natural material it was readily converted into a product, ı. p. 246—247°, identical with the usual form of the vitamin. The m. p. of aneurin hloride hydrochloride is not a very good criterion of purity, as m. p.'s ranging from 245° ) 250° can be obtained according to the rate of heating. The possibility that our low-ıelting material is contaminated with *O*-acetylaneurin is unlikely, as treatment of it with queous picric acid yields at once a crystalline picrate, m. p. 203—204° without further urification. In our experience direct production of a crystalline picrate of this m. p. is nly possible with very pure aneurin. Moreover, the same low-melting form of the vitamin as been obtained and examined by Williams and Cline (*J. Amer. Chem. Soc.*, 1937, **59**, 216) ı their synthesis of aneurin; in this case there is no possibility of acetylaneurin being resent as an impurity.

## EXPERIMENTAL.

2-*Thio*-7-*methyl*-1 : 2 : 3 : 4-*tetrahydro*-1 : 3 : 6 : 8-*benztetrazine* (II).—(A) A mixture of 4-nino-5-aminomethyl-2-methylpyrimidine hydrochloride (1 g.) and powdered thiourea (2 g.) as heated at 180—200° until evolution of ammonia ceased (*ca.* 2½ hours). The melt solidified ı cooling and was extracted twice with small amounts of boiling water (10 c.c.). The combined ktracts deposited, on standing, a brownish crystalline product, which was extracted with cetone, the acetone-insoluble portion being discarded. The extract was evaporated; the sidue, recrystallised from acetone–glacial acetic acid, formed faintly yellowish needles (35 mg.), . p. 272—274°. When heated with chloroacetone, it yielded a product showing strong blue ıorescence in neutral or alkaline solution.

(B) A solution of 4-amino-5-aminomethyl-2-methylpyrimidine hydrochloride (3 g.) and otassium thiocyanate (3·6 g.) in water (15 c.c.) was evaporated to dryness on the water-bath, ıd the residue extracted with absolute alcohol. After filtering from potassium chloride, the ktract was evaporated to dryness, and the residue heated at 170° for *ca.* 30 minutes. The ass at first liquefied and evolved gas, then resolidified towards the end of the heating. The oduct was cooled and twice extracted with boiling water (180 c.c. in all). The extract slowly

deposited yellowish crystals on cooling; these were collected and separated from insoluble material by extraction (Soxhlet) with acetone. The acetone extract gave on evaporation the *benztetrazine* (II), which separated from glacial acetic acid–acetone (1 : 1) in colourless soft needles, m. p. 275—277° (decomp.) (yield 1·2 g., *i.e.*, 45%) (Found in material dried at 80° : C, 46·3; H, 4·5; S, 17·4. $C_7H_8N_4S$ requires C, 46·6; H, 4·5; S, 17·8).

*Thiochrome* (I).—A mixture of the above thiobenztetrazine (1·2 g.), methyl α-chloro-γ-acetoxypropyl ketone (1·8 g.), and glacial acetic acid (16 c.c.) was heated under reflux during 10 hours. The initially clear solution began to deposit solid material after 1 hour, and after 8 hours a small amount (0·5 g.) of the chloro-ketone was added to ensure complete reaction. The mixture was cooled, excess of dry ether added, and the precipitate collected, washed with ether, dissolved in water (20 c.c.), and filtered from insoluble material (0·3 g.). Hydrochloric acid was added to the brown filtrate to give an acid concentration of 8% and after a few hours the solution was evaporated to dryness in a vacuum, and the residue washed with a little butyl alcohol, treated with alcoholic potassium hydroxide solution (15 c.c. of 20%), and extracted rapidly with chloroform (*ca.* 2 l.). The blue-fluorescent chloroform extract was dried and evaporated in a vacuum to *ca.* 50 c.c. Thiochrome slowly separated in faintly yellow, flaky crystals. Recrystallised from chloroform, it had m. p. 224—225°, undepressed by thiochrome prepared by oxidation of natural aneurin (yield, 0·22 g.) (Found : C, 55·5; H, 5·6. Calc. for $C_{12}H_{14}ON_4S$ : C, 54·9; H, 5·3%).

When treatment of the crude product with hydrochloric acid was omitted, a product, m. p. 203°, probably acetylthiochrome, was sometimes obtained.

*Synthesis of Aneurin : Isolation of* O-*Acetylaneurin.*—A mixture of 4-amino-5-thioformamidomethyl-2-methylpyrimidine (1 g.), methyl α-chloro-γ-acetoxypropyl ketone (1·2 g.), and glacial acetic acid (5 drops) was heated at 118—119° for 25 minutes; the mixture, at first liquid, became viscous. After cooling, the product was washed with ether and warmed with absolute alcohol (8 c.c.) containing alcoholic hydrogen chloride (1 c.c. of 4%). After standing for 12 honrs, the crystalline hygroscopic material (0·5 g.) was collected and redissolved in absolute alcohol (5 c.c.) containing a trace of hydrogen chloride. In the course of several hours O-*acetylaneurin chloride hydrochloride* (0·1 g.) separated; recrystallised from absolute alcohol, it formed colourless leaflets, m. p. 205—207° (Found in material dried at 40°: N, 13·7. $C_{14}H_{19}O_2N_4SCl,HCl,H_2O$ requires N, 14·1%). The picrate had m. p. 176°. When a larger concentration of hydrogen chloride than the above-mentioned was used in preliminary treatment of the reaction mixture, only traces of acetylaneurin were obtained.

From the acetylaneurin mother-liquors and from the original mother-liquor more solid material separated on standing. Repeated crystallisation from absolute alcohol containing hydrogen chloride gave aneurin chloride hydrochloride, m. p. 236—237°, indistinguishable save in m. p. from the natural vitamin.

THE LISTER INSTITUTE, LONDON. [*Received, November 26th, 1937.*]

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## 8. *Direct Introduction of Deuterium into the Aromatic Nucleus. Part II. Orientation by Certain Substituents.*

By ARTHUR P. BEST and CHRISTOPHER L. WILSON.

a..
in 1 In agreement with the hypothesis that nuclear deuteration in aromatic compounds
chlor. electrophilic substitution, it has been shown that phenol and aniline are sub-
'ed exclusively in the ortho- and para-positions.

THE structure
B1), has been esta hat aromatic deuteration is an electrophilic substitution is supported by
and 2-amino-4-met nental evidence concerning relative velocities of nuclear exchange in
Jacob, J., 1936, 1601 ited benzenes (Ingold, Raisin, and Wilson, J., 1936, 1637). It has
for the preparation of tituents which accelerate deuteration are those which are known to
various purposes, we er coupling processes. For example, hydrochloric acid, under
synthesis of 3-methylt, induced considerable nuclear exchange in dimethylaniline,
69, 217). 2-Thio-7-met ole, and none at all in benzene.
with methyl α-chloro-γ-d that substituents such as the dimethylamino- or methoxy-group
acetic acid; a product substitution principally by activation of the ortho- and para-

positions. In compounds containing such groups deuteration should, therefore, cease or almost cease when these three nuclear positions are exchanged. It is known that three and only three nuclear positions are exchanged with facility in anisole, phenol (*idem, ibid.* Cf. also Small and Wolfenden, J., 1936, 1811), dimethylaniline (Kharasch, Brown, and McNab, *J. Org. Chem.*, 1937, **2**, 41), and aniline (Harada and Titani, *Bull. Chem. Soc. Japan*, 1936, **11**, 554) and in each of these instances it has been assumed (*locc. cit.*), without direct proof, that the deuterium enters the ortho- and para-positions. We have therefore oriented deuterated phenol and aniline by converting each into a **1 : 3 : 5**-tribromo-derivative. The latter was free from deuterium, thus demonstrating that, under the conditions of exchange, the meta-positions remain unaffected.

## Experimental.

*Phenol.*—Phenol (15 g.), sodium hydroxide (3 g.), and dilute deuterium oxide (excess density 2141 p.p.m., 74 g.) were heated in a sealed bulb at 100° for 96 hours. It has already been shown (Ingold, Raisin, and Wilson, *loc. cit.*) that under these conditions the hydrogen of the phenol, reckoned as a whole, attains an isotopic composition corresponding with about 900 p.p.m. in excess water density. The alkaline solution from the above experiment was acidified, and the phenol precipitated with bromine water. The tribromophenol was filtered off, dissolved in ether, and shaken with distilled tap water to 'normalise' the hydroxyl hydrogen, and then dried and burnt in the usual manner. The water produced had the same density as the standard water to within the limit of accuracy of the pyknometer (1 p.p.m.).

*Aniline.*—Harada and Titani (*loc. cit.*) have described nuclear exchange between water and aniline hydrochloride. The latter (26 g.) and water (excess density 2141 p.p.m., 36 g.) were heated at 100° in a sealed bulb for 30 hours. The solvent was evaporated in a vacuum, the residue dissolved in 'normal' water and made alkaline, and the aniline was extracted with ether. The ethereal solution was further shaken with 'normal' water, and the aniline distilled. Half of it was burnt, giving water which had an excess density of 599 p.p.m., and the remainder was dissolved in acid and converted into the tribromo-derivative. Combustion of the latter gave a water sample having a density 1 p.p.m. less than the standard.

The authors are indebted to Professor C. K. Ingold, D.Sc., F.R.S., for advice and thank the Chemical Society for a grant.

The Sir William Ramsay and Ralph Forster Laboratories,
*University College, London.* [*Received, December 11th, 1937.*]

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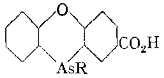
# 9. *The Configuration of Heterocyclic Compounds. Part VI. An Examination of Derivatives of Selenoxanthone and Phenoxselenine.*

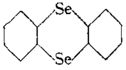
By Mary C. Thompson and E. E. Turner.

Suitably substituted phenoxarsines are capable of exhibiting optical activity. This is probably due to the fact that the molecule is folded about the oxygen–arsenic axis. The folding has previously been thought to be stabilised as a result of the dissimilarity in size and valency angle of oxygen and arsenic. Phenoxselenines would therefore be expected to have a similar configuration and thus be able, if suitably substituted, to exhibit optical activity. The experiments now described indicate, however, that neither phenoxselenines nor selenoxanthones, which should also be folded, can be obtained in mirror-image forms. The fact that negative evidence is not conclusive is appreciated.

The optical activity of 10-substituted phenoxarsine-2-carboxylic acids (I) (Lesslie and Turner, J., 1934, 1178; 1935, 1268; 1936, 730) has been explained as being due to a folded configuration of the molecule, stabilised as a result of the particular sizes of the atomic radii and the valency angles of oxygen and arsenic. The non-resolvability of certain derivatives of thianthren, a substance known to have a folded structure (Bergmann and Tschudnowsky, *Ber.*, 1932, **65**, 458; Bennett and Glasstone, J., 1934, 128) and of

similar derivatives of phenoxthionine (Bennett, Lesslie, and Turner, J., 1937, 444) has been attributed to the identity in size of the sulphur atoms in the one case and the

(I.) 

 (II.)

insufficient dissimilarity in size of the oxygen and sulphur atoms in the other (compare also Keats, J., 1937, 1592).

In phenoxselenine, the factors which at any rate might be regarded as stabilising the folding of the phenoxarsine molecule would appear to be reproduced, since the arsenic and the selenium atom have approximately the same radius; the absence of a substituent in position 10 in phenoxselenines makes them particularly important material for investigation.

The literature contains little information as to the valency angle of selenium. Bergmann, Engel, and Sandor (*Z. physikal. Chem.*, 1930, *B*, **10**, 397) found the dipole moment of diphenyl selenide to be $1\cdot38 \times 10^{-18}$ e.s.u., from which it might be inferred, although the difficulties of making correct inferences are well known, that selenium has a preferred valency angle larger than that of sulphur, which is considerably less than 120° (Bennett and Glasstone, *loc. cit.*). The dipole moment of selenanthren (II) (Krafft and Kaschau, *Ber.*, 1896, **29**, 443) has now been found by Le Fèvre and Le Fèvre to be $1\cdot43 \times 10^{-18}$ (see Campbell, Le Fèvre, Le Fèvre, and Turner, forthcoming publication) showing that the selenanthren molecule is folded like the thianthren molecule and to a similar extent, and suggesting that the valency angle of selenium is in the neighbourhood of 110°.

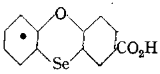
The radii of aromatic carbon, of oxygen, and of selenium being assumed to be respectively 0·70, 0·66, and 1·17 A., the relation between the oxygen angle, θ, the selenium angle, $\phi$, and the angle, $\psi$, of fold about the oxygen–selenium axis may be calculated and is as follows:

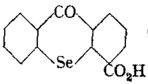
| | | | | | |
|---|---|---|---|---|---|
| θ ........................................ | 100·0° | 110·0° | 120·0° | 130·0° | 136·5° |
| $\phi$ ........................................ | 80·5 | 87·5 | 94·0 | 100·0 | 103·5 |
| $\psi$ ........................................ | 111·0 | 123·5 | 137·5 | 154·5 | 180·0 |

The calculation is based on the assumption that, in all possible configurations, the centres of the oxygen and selenium atoms remain in the planes of the two benzene nuclei, and that the oxygen–carbon and selenium–carbon bonds make angles of 120° with the adjacent aromatic nuclear bonds.

In some diaryl ethers the oxygen valency angle reaches as high a value as 128°±4° (Sutton and Hampson, *Trans. Faraday Soc.*, 1935, **31**, 945; cf. Maxwell, Hendricks, and Mosley, *J. Chem. Physics*, 1935, **3**, 669; Pai, *Indian J. Physics*, 1935, **3**, 660; Sutton and Brockway, *J. Amer. Chem. Soc.*, 1935, **57**, 473: these authors find angles somewhat lower). There seems little doubt that the value of θ in the example under review may be taken as something a little greater than 120°, a value it acquires in diphenylene dioxide in which 120° is the maximum possible angle (Bennett and Glasstone, J., 1934, 1179). It appears probable, therefore, that since selenium is a "softer" atom than oxygen, $\phi$ will give way to θ, so that $\psi$ will be of the order of 140—150°.

We have synthesised *phenoxselenine-2-carboxylic acid* (III) and attempted its resolution. The strychnine, morphine, cinchonine, and quinidine salts of this acid were unsuitable for examination, but the *cinchonidine*, d- and l-*phenylethylamine*, and *brucine*

(III.) 

 (IV).

salts were well defined. The cinchonidine salt showed no signs of resolving when it was crystallised from alcohol: 12 crops were examined polarimetrically, and had $[\alpha]_{5791}^{20°}$ — 64·1°

to $-$ 66·5°, $[\alpha]_{5461}^{20°}$ $-$ 72·6° to $-$ 76·0°, in chloroform (*c*, *ca.* 1·3). The *d*- and the *l*-α-phenylethylamine salt were fractionally crystallised from alcohol; 7 crops of the salt of the *l*-base and four of that of the *d*-base had no appreciable numerical difference in specific rotation. The brucine salt was fractionally crystallised a very large number of times and the specific rotations of 13 crops were determined: the values of $[\alpha]_{5791}^{20°}$ varied from $-$ 10·3° to $-$ 6·2°, and of $[\alpha]_{5461}^{20°}$ from $-$ 12·8° to $-$ 7·4° (acetone solution), but owing to the smallness of the observed angle (0·3—0·4°) the experimental error was considerable, and the free acids liberated from the salts were invariably inactive. Moreover, none of the solutions of the salts exhibited mutarotation and no asymmetric induction effects could be detected. The inactivity of the acids liberated from different crops cannot therefore be ascribed to swift racemisation.

6 : 8-*Dichlorophenoxselenine-2-carboxylic acid* has also been synthesised, but it proved unsuitable for resolution experiments. The acid formed very unstable salts with strychnine, brucine, quinine, cinchonine, and cinchonidine, and even with nor-*d*-ψ-ephedrine. The d-α-*phenylethylamine* salt was stable, but showed no signs of resolving when it was repeatedly crystallised.

Attempts were made to prepare a nitro-derivative of phenoxselenine-2-carboxylic acid, but conditions for effecting satisfactory nitration could not be found. A synthesis of a dimethyl derivative of the acid failed at an intermediate stage.

Selenoxanthone (aliphatic carbon radius 0·77 A.) would be expected to have a folded configuration, as the following table shows:

| | | | | | |
|---|---|---|---|---|---|
| Carbon angle, θ | 100·0° | 110·0° | 120·0° | 130·0° | 133·0° |
| Selenium angle, φ | 84·5 | 92·0 | 98·5 | 105·5 | 107·0 |
| Angle of fold, ψ | 113·5 | 126·5 | 142·0 | 163·0 | 180·0 |

since it is improbable that carbon would tolerate a valency angle exceeding 125°. We have therefore attempted to resolve selenoxanthone-1-carboxylic acid (IV), prepared by Lesser's method (*Ber.*, 1914, **47**, 2515). The brucine, nor-*d*-ψ-ephedrine, *l*-α-phenylethylamine, and *strychnine* salts were prepared. The last was fractionally crystallised from acetone. In one set of experiments twenty, and in another sixteen, crops were examined polarimetrically; no evidence of resolution was obtained, and the investigation was complicated by the tendency for free strychnine to separate. Decomposition of the various crops gave optically inactive acids.

Although negative evidence is never satisfactory, our examination of the salts of phenoxselenine-2-carboxylic acid was so prolonged that we think it extremely improbable that this acid can be resolved. Until further examples of optical activity due to folding are discovered, no conclusions can be drawn as to the effect of the degree of folding on the dissimilarity in diastereoisomeric pairs of salts, but it is possible that when ψ approaches 180°, even when the molecule is rigidly folded, resolution fails because the diastereoisomerides differ insufficiently in solubility. Alternatively, of course, a non-resolution may be due to the flexibility of the folded molecule.

Comparison of the (assumed) optical instability of the phenoxselenines with the (known) optical stability of the phenoxarsines suggests that one reason for the difference is that in the former the selenium atom has two pairs of unshared electrons as against an attached group and one pair of unshared electrons in the case of the arsenic atom. The increased moment of inertia due to the attached group must make a definite contribution to the stability of the configuration of the arsenic atom and therefore indirectly to that of the whole molecule.

Since no selenoxide has yet been resolved, although on theoretical grounds selenoxides should be capable of exhibiting optical activity, we have attempted the resolution of 2-*carboxyphenoxselenine* 10-*oxide* (VII). Gaythwaite, Kenyon, and Phillips (*J.*, 1928, 2280) found that 4-carboxydiphenyl and carboxyphenyl methyl selenoxides underwent partial reduction to selenides during the formation of certain alkaloidal salts, and we obtained a similar result in attempting to resolve the *l*-α-phenylethylamine, strychnine, and brucine salts of 2-carboxyphenoxselenine 10-oxide. The *nor*-d-ψ-*ephedrine* salt of this acid crystallised satisfactorily from water, but its specific rotation was unaffected by

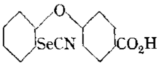
repeated crystallisation, $[\alpha]^{20^\circ}_{5791}$ varying only from + 16·7° to + 17·4°, a variation not exceeding the unavoidable experimental error.

At the outset of this investigation four years ago, the only known phenoxselenine was the parent substance, obtained by Drew (J., 1928, **511**) by heating phenoxtellurine with selenium, and various possible routes to this series had therefore to be explored.

Although sulphur reacts with diphenyl ether in presence of aluminium chloride, selenium could not be caused to do so, probably owing in part to the insolubility of selenium in the ether.

As is known, sulphones react with selenium at high temperatures to give selenides, and even thianthren 5 : 5 : 10 : 10-tetraoxide is slowly converted into selenanthren when it is boiled in presence of selenium (Krafft and Kaschau, *loc. cit.*). Yet phenoxthionine 10 : 10-dioxide could not be made to react with selenium and give phenoxselenine.

A new synthesis of phenoxselenines has therefore been worked out, in particular one leading to carboxylic acids. Preliminary experiments showed that the amino-group in 2-aminophenyl *p*-tolyl ether could be replaced by the selenocyanate group (Bauer, *Ber.*,



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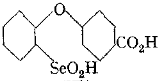

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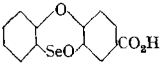
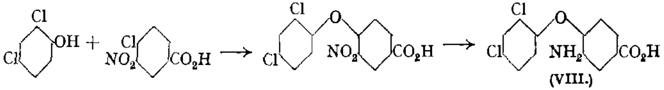


(VII.)

1913, **46**, 92), but it was found impractible to oxidise the selenocyano-derivative satisfactorily. The amino-ether was therefore acetylated and oxidised, and the product hydrolysed. The resulting *4'-carboxy-2-selenocyanodiphenyl ether* (V) was then oxidised with diluted nitric acid (Challenger and Peters, J., 1928, 1366) to *4'-carboxydiphenyl ether 2-seleninic acid* (VI). Ring-closure of this acid to *2-carboxyphenoxselenine 10-oxide* (VII) could not be effected by using concentrated sulphuric acid at 100°, but with 85% acid at 40° it took place readily, and reduction of the product with potassium anhydrosulphite gave phenoxselenine-2-carboxylic acid (III). Decarboxylation of this acid gave phenoxselenine. The selenoxide acid, which is most readily obtained by first isolating phenoxseleninecarboxylic acid and then oxidising it with hydrogen peroxide (Drew, *loc. cit.*), loses oxygen at its melting point, giving the parent acid.

The synthesis employed for 6 : 8-dichlorophenoxselenine-2-carboxylic acid was similar in the last stages to that of the parent acid, but the *amino*-compound (VIII) was obtained according to the scheme :



(VIII.)

## Experimental.

*2-Selenocyano-4'-methyldiphenyl Ether.*—2-Amino-4'-methyldiphenyl ether (59 g.; 1 mol.) was diazotised, and the filtered solution then treated with sodium acetate until it was no longer acid to Congo-red. The solution was added slowly (15 mins.) to 110 c.c. of a 50% solution of potassium selenocyanate (1·5 mol.). The commercial selenocyanate was used, or a solution was prepared by a simplification of the method of Muthmann and Schröder (*Ber.*, 1900, **33**, 1765) without isolating the solid. A reaction ensued at once and was allowed to become complete at the ordinary temperature. The dark red oil which separated was extracted with chloroform, the extract dried over calcium chloride, and the solvent removed. Distillation gave only 4 g. of 2-selenocyano-4'-methyldiphenyl ether, b. p. 224—227°/18 mm., which later solidified and then separated from alcohol in crystals, m. p. 46°. These became pink when left in air. Several attempts to oxidise the crude selenocyano-compound with various concentrations of nitric acid led to inseparable mixtures.

*2-Acetamido-4'-methyldiphenyl Ether.*—Crude 2-amino-4'-methyldiphenyl ether, obtained as an oil by reduction of the corresponding nitro-compound with iron and acidified water, was poured into a solution of twice the calculated quantity of acetic anhydride in water. The

mixture was warmed gently until crystals of the *acetyl* compound separated, and was then poured into much water, and the precipitate filtered off, dried, and crystallised from light petroleum (b.p. 80—100°), from which it separated in needles or prisms, m. p. 92° (Found: N, 6·0. $C_{15}H_{15}O_2N$ requires N, 5·8%).

*2-Acetamido-4'-carboxydiphenyl Ether.*—A suspension of 2-acetamido-4'-methyldiphenyl ether (24 g., 1 mol.) in a solution of magnesium sulphate heptahydrate (50 g., 2 mols.) in 1500 c.c. of water was treated (with mechanical stirring) at 85—90° with potassium permanganate (64 g., 2 mols.), added in small quantities during 2 hours. The reaction mixture was cooled and decolorised with sulphur dioxide, the precipitate formed being filtered off and dissolved in sodium carbonate. After filtration from a small amount of alkali-insoluble material, the solution was acidified with concentrated hydrochloric acid. Yield, 22·5 g. (83%). The *acetamido-acid* so obtained formed short rods, m. p. 211°, from alcohol (Found: N, 5·1. $C_{15}H_{13}O_4N$ requires N, 5·2%).

*2-Amino-4'-carboxydiphenyl Ether.*—A suspension of 5 g. of the acetamido-acid in 60 c.c. of 20% hydrochloric acid was boiled for ¾ hour. The original heavy powder was gradually replaced by a matte of feathery needles of the hydrochloride, from which the base was liberated by means of concentrated sodium acetate solution. The *2-amino-4'-carboxydiphenyl ether* crystallised from alcohol in square or rectangular prisms, m. p. 137° (Found: N, 6·1. $C_{13}H_{11}O_3N$ requires N, 6·1%). Mayer and Krieger (*Ber.*, 1922, **55**, 1663) state that the acid melts at 120—121°, but give no analysis.

*2-Selenocyano-4'-carboxydiphenyl Ether.*—The amino-acid hydrochloride (26 g.) was diazotised, and the solution rendered non-acid to Congo-red by addition of sodium acetate. It was then added gradually to 40 c.c. of 50% potassium selenocyanate solution, kept at 0°. Evolution of nitrogen occurred, and was complete after ¾ hour at the ordinary temperature, followed by a short heating at 100°. The cooled mixture was filtered, and the red solid obtained extracted several times with sodium bicarbonate. The first extraction gave dark-coloured acids on acidification, but the later ones gave rise to pale yellowish-brown acids. The *2-selenocyano-4'-carboxydiphenyl ether* proved difficult to crystallise, but from light petroleum (b. p. 100—120°) pale brownish needles, m. p. 178°, were obtained (Found: C, 53·4; H, 2·9. $C_{14}H_9O_3NSe$ requires C, 52·8; H, 2·85%). The yield of crude acid was 80%.

*4'-Carboxydiphenyl Ether 2-Seleninic Acid.*—A solution of the selenocyano-acid (3 g.) in 90 c.c. of 33% nitric acid solution was boiled for a few minutes and then cooled. Some tar and selenium separated and were removed. On addition of an equal volume of water, the *carboxyseleninic acid* was deposited on standing. After being twice crystallised from glacial acetic acid, it had m. p. 212° (decomp.) (yield, 35%) (Found: C, 47·9; H, 3·35. $C_{13}H_{10}O_5Se$ requires C, 47·95; H, 3·1%). From nitric acid (*d* 1·4) the seleninic acid crystallised as a nitrate, decomposing at 120—130°.

*Phenoxselenine-2-carboxylic Acid.*—A large number of experiments were performed before conditions were found for effecting ring-closure of the carboxyseleninic acid. With concentrated sulphuric acid, deep blue products were formed owing no doubt to selenylium salt formation such as Drew observed (J., 1928, 511). The following method gave an 80% yield of the desired phenoxselenine oxide acid; 5 g. of carboxyseleninic acid were gradually added to 36 c.c. of 85% sulphuric acid at 0°. The dark green solution obtained was heated at 40—45° for 40 minutes and then poured on ice. The precipitate was contaminated with small quantities of the above-mentioned blue compounds, but these were removed on thorough washing with water. The crude 2-carboxyphenoxselenine 10-oxide so obtained was ground with one part of potassium metabisulphite and a little water. After an hour, the mixture was filtered and the *phenoxselenine-2-carboxylic acid* crystallised from alcohol or benzene. It formed pale yellow needles, m. p. 251° (Found: C, 53·4; H, 2·9. $C_{13}H_8O_3Se$ requires C, 53·6; H, 2·8%). The sodium salt of the acid is sparingly soluble in cold, but readily soluble in hot, water. When bromine is added to a solution of the acid in glacial acetic acid, orange-red plates of the unstable *dibromide*, m. p. 214° (decomp.), are precipitated (Found: Br, 33·7. $C_{13}H_8O_3Br_2Se$ requires Br, 35·4%). Cold water at once converts the dibromide into the selenoxide acid. When the carboxyphenoxyseleninic acid was added to concentrated sulphuric acid at 0°, a red solution, becoming olive-green, was obtained. Heating this solution at 100° for 20 minutes caused the separation of a blue-black precipitate, and treatment with water, followed by crystallisation from glacial acetic acid or benzene, gave a small yield of the phenoxseleninecarboxylic acid (Found: C, 53·3; H, 3·0%) and none of the selenoxide acid. The carboxyphenoxyseleninic acid was unaffected by heating with 75% sulphuric acid at 100° for 15 minutes.

*Decarboxylation of Phenoxselenine-2-carboxylic Acid.*—A solution of 1 g. of this acid in 30 c.c. of quinoline, to which a little copper bronze had been added, was boiled for ¾ hour. The mixture was poured into dilute hydrochloric acid, and the precipitate collected and warmed with dilute aqueous sodium hydroxide solution. The undissolved solid was crystallised from alcohol, phenoxselenine being obtained, m. p. 87° alone or when mixed with a specimen kindly supplied by Dr. H. D. K. Drew.

*Experiments on the Resolution of Phenoxselenine-2-carboxylic Acid.*—(a) *With cinchonidine.* The *cinchonidine* salt crystallised readily as prisms m. p. 211° when the base was added to an equivalent amount of the acid in hot alcohol (Found: C, 66·3; H, 5·3. $C_{32}H_{30}O_4N_2Se$ requires C, 65·6; H, 5·2%); it was crystallised repeatedly from this solvent, but all the crops had the same specific rotation within the limits of experimental error (see p. 30).

(b) *With* d- *and* l-*α-phenylethylamine.* Slightly more than the calculated equivalent of base was added to a hot ethyl-alcoholic solution of the acid. Prisms separated, m. p. 207°. The salt was insoluble in acetone and in chloroform, slightly soluble in hot water, and soluble in absolute methyl alcohol. It was crystallised repeatedly from alcohol, but showed no appreciable change in specific rotation. The *l*-base *salt* (Found: C, 60·7; H, 4·7. $C_{21}H_{19}O_3NSe$ requires C, 61·15; H, 4·7%) had $[\alpha]^{20°}_{5791}$ − 3·5°, $[\alpha]^{20°}_{5461}$ − 3·8°; the *d*-base salt had $[\alpha]^{20°}_{5791}$ + 3·7°, $[\alpha]^{20°}_{5461}$ + 4·2°, in methyl alcohol (*c* about 2).

(c) *With brucine.* A hot ethyl-alcoholic solution of 14·55 g. of acid was treated with 1 equiv. (21·5 g.) of brucine dihydrate. On cooling, 27 g. of needles separated; $[\alpha]^{20°}_{5791}$ − 9·7°, $[\alpha]^{20°}_{5461}$ − 11·9° ($c = 2·012$, in acetone). This salt was repeatedly crystallised from ethyl alcohol, and the crops had the rotations given on p. 31, but the acids liberated from different specimens of salt were all inactive. The specific rotation of the brucine salt varies considerably with concentration, $[\alpha]^{20°}_{5791}$ being − 8·5° and − 5·9° for $c$ = 1·7 and 2·2 respectively. The brucine salt separates in prisms from alcoholic solution (under ordinary conditions of crystallisation) as a *trihydrate* (Found: C, 58·1; H, 5·5; $H_2O$, 7·0. $C_{36}H_{34}O_7N_2Se,3H_2O$ requires C, 58·4; H, 5·5, $H_2O$, 7·3%). From absolute alcohol only a gum separates.

*Experiments on the Resolution of Selenoxanthone-*1*-carboxylic Acid.*—The acid was prepared by Lesser's method (*loc. cit.*) (Found: C, 55·25; H, 2·8. Calc.: C, 55·4; H, 2·7%).

The *l*-α-phenylethylamine salt was obtained by boiling a suspension of 42·4 g. of the acid in 3 l. of alcohol containing 16·9 g. of *l*-α-phenylethylamine. On cooling the filtered solution, 55 g. of yellow prisms separated. The salt was almost insoluble in benzene, chloroform, and ethyl acetate, and although moderately soluble in hot was virtually insoluble in cold alcohol. Fractional crystallisation from ethylene glycol was practicable, but crops which separated were dark and were crystallised from alcohol before being examined polarimetrically: $\alpha_{5791}$ = − 0·01° and − 0·08° ($c = 1·5$; $l = 2$; in ethylene glycol) for all the crops. The *strychnine* salt, prepared similarly, could only be crystallised from acetone. It was microcrystalline, and after being dried to constant weight at 100° and then in a high vacuum had m. p. 240—243° (Found: Se, 12·25. $C_{35}H_{30}O_5N_2Se$ requires Se, 12·4%). Two separate sets of fractional crystallisations were carried out, and although 36 crops were examined polarimetrically, no evidence for resolution was obtained. Free strychnine sometimes separated with the salt, which has $[\alpha]^{20°}_{5461}$ + 3·5° (in chloroform). Samples of acid liberated from crops having rotations somewhat different from this figure were inactive.

2′ : 4′*-Dichloro-2-nitro-4-carboxydiphenyl Ether.*—Potassium hydroxide (60 g.) was melted in presence of 5 drops of water, and 50 g. of 2 : 4-dichlorophenol added. To the clear melt 80 g. of 4-chloro-3-nitrobenzoic acid were added, and the whole boiled for 1·5 hours at 175—180°. The mixture was treated with water, and then saturated with carbon dioxide. The phenol which separated was removed, and that remaining in solution was extracted with ether. Acidification of the aqueous layer precipitated the *acid*, which was microcrystalline from alcohol and had m. p. 207—209° (yield, 54%) (Found: Cl, 21·7. $C_{13}H_7O_5NCl_2$ requires Cl, 21·6%).

2′ : 4′*-Dichloro-2-amino-4-carboxydiphenyl Ether.*—The nitro-acid (26 g.) was dissolved in a mixture of 120 c.c. of ammonia (*d* 0·880) and 240 c.c. of water. A concentrated solution of 224 g. of ferrous sulphate crystals was added, and the mixture boiled for 10 minutes. The black precipitate was extracted with boiling dilute sodium hydroxide. The filtered extract, when slightly acidified and treated with sodium acetate, gave the *amino-acid*, which separated from alcohol in blunt prisms, m. p. 199° (yield, 80—90%) (Found: Cl, 23·6. $C_{13}H_9O_3NCl_2$ requires Cl, 23·8%). The acid was alternatively obtained by catalytic reduction in alcoholic solution in presence of platinum. The product was more easily worked up, but the yield was less satisfactory. The *acetyl* derivative of the acid formed long prisms, m. p. 232°, from alcohol (Found: Cl, 20·7. $C_{15}H_{11}O_4NCl_2$ requires Cl, 20·85%).

2′ : 4′-*Dichloro-2-selenocyano-4-carboxydiphenyl Ether.*—The amino-acid was diazotised in hydrochloric acid, and the solution added to a 50% solution of potassium selenocyanate at 0°. The whole was kept at 40° for 2 hours (or cold overnight), and then heated at 100° until nitrogen was no longer evolved. The brown precipitate was extracted twice with cold sodium bicarbonate solution, and then with the warm reagent. Acidification of the cold extracts gave tars, but that of the warm extracts afforded the *selenocyano*-compound. This crystallised from alcohol in brown plates, m. p. 247—248° (decomp.) (Found : Cl, 18·4. $C_{14}H_7O_3NCl_2Se$ requires Cl, 18·3%).

2′ : 4′-*Dichloro-4-carboxydiphenyl Ether 2-Seleninic Acid.*—A mixture of 9 g. of the selenocyano-ether and 330 c.c. of 52% nitric acid was boiled for 40 minutes under reflux, and then cooled and filtered from tar. On addition of the solution to 2 vols. of water, the *seleninic acid* was precipitated. It crystallised from aqueous alcohol in slender needles, softening about 176° and gradually decomposing when heated above this temperature (Found : Cl, 17·8. $C_{13}H_8O_5Cl_2Se$ requires Cl, 18·0%) (yield, 50%). The acid dissolves in concentrated sulphuric acid to a deep blue solution, whereas the chlorine-free acid gives a purple colour under similar conditions.

6 : 8-*Dichlorophenoxselenine-2-carboxylic Acid.*—Ring-closure of the seleninic acid could not be effected with 85% sulphuric acid at 40° as in the preparation of the parent acid, but took place to the extent of 90% under the following conditions. The seleninic acid (5 g.) was gradually added to 50 c.c. of concentrated sulphuric acid at 0°. The blue mixture was allowed to acquire room temperature during ½ hour, and then became dark red. On pouring the solution on ice, a white or pale green solid separated, which was treated with a cold saturated solution of potassium anhydrosulphite for ½ hour. The *acid* so obtained crystallised from a large bulk of glacial acetic acid or from dioxan in slender needles, m. p. 309° (Found : Cl, 20·0. $C_{13}H_6O_3Cl_2Se$ requires Cl, 19·9%). The sodium and ammonium salts were soluble in hot water, the solutions becoming gels when cooled.

The d-*α-phenylethylamine salt* was obtained by dissolving the acid in a boiling alcoholic solution of the base. It forms prisms, softening at 186° and melting indefinitely at 250—265° (Found : Cl, 14·6. $C_{21}H_{17}O_3Cl_2NSe$ requires Cl, 14·7%). Fractional crystallisation of the salt from alcohol gave a number of crops having $[\alpha]_{5791}^{20°}$ + 4·2° in alcohol. Samples of acid liberated from the salts were inactive.

5 : 5′-*Dicarboxy-2* : 2′-*di-(2′ : 4′-dichlorophenoxy)diphenyl diselenide* was prepared either (*a*) by boiling a solution of the selenocyano-acid in dilute sodium hydroxide for 10 minutes, or (*b*) by reducing the seleninic acid with potassium anhydrosulphite. It crystallises with 2 molecules of solvent from glacial acetic acid in pale yellow needles, m. p. 278° (decomp.) (Found : Cl, 16·9. $C_{26}H_{14}O_6Cl_4Se_2,2C_2H_4O_2$ requires Cl, 16·9%). The unsolvated *acid* was obtained by precipitating an alkaline solution with dilute hydrochloric acid, followed by vacuum drying (Found : Cl, 19·7. $C_{26}H_{14}O_6Cl_4Se_2$ requires Cl, 19·6%).

*Nitration of* o-*Nitrophenyl* p-*Tolyl Ether.*—The ether (5 g.) was added to a mixture of 50 g. of nitric acid (*d* 1·5) and 50 g. of glacial acetic acid. The warm mixture was heated to 100°, and at once poured into water. Crystallisation of the precipitate from alcohol gave 2 : 2′-dinitro-4-methyldiphenyl ether, m. p. 106°. Since Cook (*Amer. Chem. J.*, 1901, **25**, 64) gave the m. p. as 100°, and did not prove the constitution, we heated the dinitro-compound with piperidine and isolated *o*-nitrophenylpiperidine and 3-nitro-*p*-cresol, thereby establishing the position of the second nitro-group.

*Preparation of 4-Chloro-3-nitrobenzoic Acid.*—The following modification of the method described by Hübner (*Z. Chem.*, 1866, 615) proved excellent : 20 g. of *p*-chlorobenzoic acid were added gradually to 140 c.c. of nitric acid (*d* 1·5), the temperature being kept below 30°. The solution was heated to 55—60° for 10 minutes, and poured into water. The acid, after crystallisation from aqueous alcohol, was pure, m. p. 184°. Yield 96%.

2-*Nitro-4-carboxy-3′* : 5′-*dimethyldiphenyl Ether.*—Potassium hydroxide (15 g.) was melted in presence of 3 drops of water and 37 g. of *m*-xylenol were added. To the clear melt, 20 g. of 4-chloro-3-nitrobenzoic acid were added, and the mixture was heated at 170—180° for 1½ hours. The cooled product was treated with 500 c.c. of water, and then saturated with carbon dioxide. The xylenol which separated was removed, and that remaining in solution was extracted with ether. The aqueous solution was acidified, and the precipitated *acid* crystallised from alcohol. It forms short rods, m. p. 179—181° (yield, 20 g.) (Found : N, 4·6. $C_{15}H_{13}O_5N$ requires N, 4·9%).

2-*Amino-4-carboxy-3′* : 5′-*dimethyldiphenyl Ether.*—The nitro-acid (36 g.) was dissolved in 200 c.c. of ammonia (*d* 0·88) diluted with 200 c.c. of water. To this hot solution was added a

solution of 300 g. of ferrous sulphate crystals in 300 c.c. of acidified water. After ½ hour, the precipitate was filtered off, and the filtrate acidified. A small amount of amino-acid was then precipitated, the rest being obtained by extracting the iron precipitate with boiling dilute sodium hydroxide and acidifying the extract with hydrochloric acid. The impure hydrochloride so obtained was dissolved in water, and sodium acetate added until the solution was alkaline to Congo-red. The *amino-acid* crystallised from alcohol in short rods, m. p. 173° (Found: N, 5·5. $C_{15}H_{15}O_3N$ requires N, 5·5%) (yield, almost theoretical). The *acetyl* derivative, obtained by adding acetic anhydride to a solution of the 2-amino-compound in glacial acetic acid, separates from alcohol in slender needles, m. p. 219° (Found: N, 4·7. $C_{17}H_{17}O_4N$ requires N, 4·7%).

*2-Selenocyano-4-carboxy-3' : 5'-dimethyldiphenyl Ether.*—A solution of the amino-acid (10 g.) in one of 2 g. of sodium hydroxide in 30 c.c. of water was treated with 4 g. of sodium nitrite. The mixture was gradually added to 40 c.c. of concentrated hydrochloric acid and 40 c.c. of water, kept in a freezing mixture. Diazonium salt crystallised out during the process, and when this was complete, sodium acetate crystals were added until the solution was no longer acid to Congo-red, whereupon the diazo-salts dissolved. The filtered solution was added to 30 g. of potassium selenocyanate in 30 c.c. of water. Nitrogen was evolved, and a brown-red solid separated. The mixture was heated at 100° until nitrogen evolution ceased, and the solid, now light brown, was filtered off. The *selenocyano*-compound crystallised from alcohol in very pale brown diamond-shaped plates, m. p. 233° (decomp.) (Found: C, 55·5; H, 4·1. $C_{16}H_{13}O_3NSe$ requires C, 55·2, H, 3·8%).

*5 : 5'-Dicarboxy-2 : 2'-di-(4'-m-xylenoxy)diphenyl Diselenide.*—A solution of the selenocyano-acid in dilute sodium hydroxide was boiled for ½ hour. Acidification of the cooled solution precipitated a very hydrated acid, which was dried at 100° and crystallised from glacial acetic acid. The *diselenide-acid* (with 1 mol. of solvent) formed pale yellow plates, m. p. 239—243° (Found: C, 54·9; H, 4·5; $CH_3{\cdot}CO_2H$, 8·55. $C_{30}H_{26}O_6Se_2,C_2H_4O_2$ requires C, 54·8; H, 4·2; $C_2H_4O_2$, 8·6%). The acid forms a highly crystalline nitrate in presence of nitric acid (*d* 1·4).

*2-Carboxyphenoxselenine 10-Oxide.*—A solution of 1·8 g. of phenoxselenine-2-carboxylic acid in the least amount of hot glacial acetic acid was treated with 20 c.c. of hydrogen peroxide solution ("20-vol."). Immediate oxidation occurred and, on cooling, a microcrystalline solid separated, more being obtained by diluting the mother-liquor. The *oxide-acid* crystallised from aqueous acetic acid in needles, and melted at 217—218° to give oxygen and phenoxselenine-2-carboxylic acid. Crystallisation from glacial acetic acid gave a bright yellow compound which was apparently the diacetate, since water converted it into the oxide-acid. The latter is sparingly soluble in water and does not appear to form a dihydroxide, thereby differing from phenoxselenine 10-oxide (Drew, J., 1928, 522). The oxide-acid is sparingly soluble in methyl and ethyl alcohols and soluble in acetic acid (Found: C, 50·5; H, 2·6. $C_{13}H_8O_4Se$ requires C, 50·8; H, 2·6%).

*Attempts to Resolve 2-Carboxyphenoxselenine 10-Oxide.*—The *l*-α-phenylethylamine salt could not be prepared in a pure state. On attempting to form the strychnine and brucine salts in absolute-alcoholic solution, mixtures of the oxide-acid and phenoxseleninecarboxylic acid were obtained. The *nor-d-ψ-ephedrine salt* was, however, formed by dissolving 3·3 g. of base in 300 c.c. of hot water, adding 6·67 g. of oxide-acid and boiling until all had dissolved. On cooling slightly, iridescent prisms separated, and at the ordinary temperature cubic crystals. Both forms had m. p. 180° (softening at 175°) and the same specific rotation (Found: C, 57·8; H, 4·4. $C_{22}H_{21}O_5NSe$ requires C, 57·6; H, 3·7%). The salt was insoluble in methyl and ethyl alcohols but dissolved in the aqueous alcohols. It was insoluble in acetone, benzene, and chloroform. Repeated crystallisation from water caused no significant change in specific rotation: $[\alpha]_{5791}^{20^\circ}$ + 16·7° to + 17·4°, $[\alpha]_{5461}^{20^\circ}$ + 18·7° to + 19·7° in aqueous methyl alcohol (50%).

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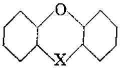
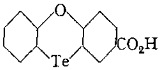
## 10. *The Configuration of Heterocyclic Compounds. Part VII. Some Derivatives of Phenoxtellurine.*

By Ishbel G. M. Campbell and E. E. Turner.

The valencies extending outwards from the six carbon atoms in benzene are in one plane with the centres of those six atoms. The radii of (combined) atoms are now known to a considerable degree of accuracy. Without making any further assumptions, it is possible to work out the probable configuration of the phenoxtellurine molecule (I, X = Te). This is shown to be least strained when it is folded about the oxygen–tellurium axis, and therefore phenoxtellurine-2-carboxylic acid (II) can be represented as existing in mirror-image forms. The calculations do not permit an estimate to be made of the stability of these folded forms, and, in fact, attempts to obtain the acid in optically active forms have failed. It is probable, therefore, that the phenoxtellurine molecule, although folded, is flexible.

The present communication describes the completion of one aspect of the investigation of the series represented by formula (I), in which X is sulphur, selenium, or tellurium,

(I.) 

 (II.)

the cases of sulphur and selenium having been dealt with already (Bennett, Lesslie, and Turner, J., 1937, 444; Thompson and Turner, preceding paper).

The following table shows the mathematical relationships existing in phenoxtellurine (I, X = Te) between the oxygen angle (θ), the tellurium angle (φ), and the consequent angle of fold (ψ), the radii of oxygen, tellurium, and aromatic carbon being taken as 0·66, 1·37, and 0·70 A., respectively :

| | | | | | | |
|---|---|---|---|---|---|---|
| θ .......................... | 90° | 110° | 120° | 130° | 140° | 142° |
| φ .......................... | 68·5 | 81·5 | 87·0 | 92·5 | 97·0 | 97·5 |
| ψ .......................... | 97·0 | 120·0 | 132·5 | 147·0 | 167·0 | 180 |

Since oxygen, when linking two aromatic nuclei, is known to prefer a valency angle somewhat greater than 120° (Sutton and Hampson, *Trans. Faraday Soc.*, 1935, **31**, 945), it is probable that ψ for the phenoxtellurine molecule lies between 135° and 145°, although this preferred, folded configuration may not be rigid. In connexion with the valency angle of tellurium, it may be noted that the dipole moments of diphenyl sulphide, selenide, and telluride are (approximately) 1·5, 1·4, and 1·1 × $10^{-18}$ e.s.u., respectively (Bergmann, Engel, and Sandor, *Z. physikal. Chem.*, 1930, *B*, **10**, 397). In the absence of information as to the dipole moment of the unknown tellurium analogue of thianthren and selenanthren, we cannot assess the valency angle of tellurium satisfactorily.

The only available test of stable configuration is the one we have applied in previous work in this series, namely, that of optical activity of suitably substituted derivatives. We have therefore attempted to resolve 2-aminophenoxtellurine and *phenoxtellurine-2-carboxylic acid* (II). The base was not very satisfactory material for investigation, but the acid gave a number of excellent salts with active bases, and because of our conviction that the essentials of our general hypothesis were correct, we only accepted the result we now publish, *viz.*, our failure to resolve the acid, when we felt that there were no further profitable experiments we could perform. Unfortunately, the method of fractional precipitation of salts is impracticable in this case, because of the relative solubilities of the acid and its salts.

2-*Aminophenoxtellurine hydrogen* d-*tartrate* was crystallised repeatedly from alcohol, and of the 30 g. of salt under examination, 14 different samples were examined polarimetrically. The salt had $[\alpha]^{20°}_{5791}$ + 2·45° in absolute ethyl alcohol, no appreciable deviations from this value being recorded. No induction effects could be produced. The recovered base was always inactive. The *d-camphorsulphonate* crystallised well from

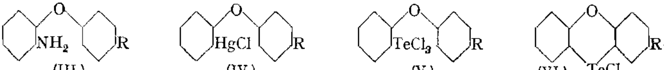
alcohol or from aqueous acetone and had $[\alpha]_{5791}^{20°}$ + 15·0° in absolute ethyl alcohol. It showed no tendency to resolve.

Phenoxtellurine-2-carboxylic acid gave a well-defined *nor*-d-*ψ-ephedrine* salt, of which 49 g. were available. Sixteen crops taken from an extended series of crystallisations were examined polarimetrically and no important deviation from $[\alpha]_{5791}^{20°}$ + 16·7° (in absolute ethyl alcohol) was recorded. The *strychnine* salt, of which 33 g. were submitted to exhaustive fractional crystallisation, had a constant value of $[\alpha]_{5791}^{20°}$ + 5·5°, in chloroform. The *quinine* salt remained unchanged although 20 g. of it were repeatedly crystallised from alcohol. It had $[\alpha]_{5791}^{20°}$ + 125° in chloroform, in which solvent it was stable only in the dark. Fractional crystallisation of 32 g. of the *cinchonidine* salt led to no appreciable change in rotation from $[\alpha]_{5791}^{20°}$ − 58·5° in absolute ethyl alcohol. The d-*α-phenylethylamine salt* (23 g.) was similarly unresolvable, having $[\alpha]_{5791}^{20°}$ + 4·0° in methyl alcohol. No specimen of acid regenerated from any crop of the salts was optically active, and no asymmetric induction effects were producible. Partial esterification of the acid with *l*-menthol did not lead to an active specimen.

We regard these results as indicating that the acid cannot be resolved, and therefore, that, although it has a folded configuration, the folding is unstable, as it is in thianthren, so that interconversion of the *d*- and the *l*-form is extremely rapid.

When this work was begun, the only phenoxtellurine derivatives known were those described by Drew (J., 1926, 223, 3054; 1927, 116), including a substance, m. p. 46—47°, which he regarded as 2-chloro-8-methylphenoxtellurine. In order to obtain a phenoxtellurinecarboxylic acid, we first condensed 4-chloro-4′-methyldiphenyl ether with tellurium tetrachloride, which, as Drew found, chlorinates phenyl *p*-tolyl ether itself. The yield of *2-chloro-8-methylphenoxtellurine*, m. p. 67—68°, was small and it was impossible to obtain a practicable method of oxidising this compound to the carboxylic acid.

After various other methods had been investigated, we succeeded in devising a convenient synthesis of phenoxtellurines. The easily prepared amino-ether (III; R = Me) was diazotised and converted into the *chloromercuri*-compound (IV; R = Me) by Nesmejanow's method (*Ber.*, 1929, 62, 1010; 1934, 67, 130). When a chloroform solution




(III.) (IV.) (V.) (VI.)

of this and tellurium tetrachloride was boiled for some time, the *telluritrichloride* (V; R = Me) was formed in good yield. This compound readily passed into *2-methylphenoxtellurine* 10 : 10-*dichloride* (VI; R = Me) when heated, and reduction of this dichloride gave *2-methylphenoxtellurine*.

Oxidation of a methyl group in a phenoxtellurine being impracticable as a route to a carboxylic acid, we applied the new synthesis to 2-amino-4′-carboxydiphenyl ether (III; R = $CO_2H$). The process worked excellently, provided acetonitrile was used as solvent for the reaction (IV) ⟶ (V).

## Experimental.

*2-Nitrophenoxtellurine.*—Phenoxtellurine (50 g.), prepared by Drew's method (*loc. cit.*), was gradually added to a mixture of 330 c.c. of nitric acid (*d* 1·5) and 500 c.c. of glacial acetic acid at the ordinary temperature. The mixture was heated on the boiling water-bath until the dinitrate had completely dissolved (1½ hours), and the solution was then poured into much water containing ice. The precipitated dinitrate was immediately reduced with 60 g. of potassium anhydrosulphite and 200 c.c. of water. The gummy mass obtained was extracted with chloroform and the extract was dried and evaporated. The residue, when crystallised from alcohol–acetone, gave 11·5 g. of pure 2-nitrophenoxtellurine as yellow needles, m. p. 128—129°.

2-Aminophenoxtellurine could not be obtained by catalytic reduction under pressure, apparently owing to poisoning of the platinum oxide used, but was prepared in 65% yield by Drew's method (*loc. cit.*).

*2-Aminophenoxtellurine Hydrogen* d-*Tartrate*.—A solution of 10 g. of tartaric acid in 100 c.c. of absolute alcohol was added to one of 20·7 g. of aminophenoxtellurine in 350 c.c. of hot absolute alcohol. On cooling, 24·2 g. of the *salt* separated as rosettes of small flat needles, and on concentrating the mother-liquor two further crops of 4 g. and 2 g., severally. These crops had $[\alpha]_{5791}^{20^\circ}$ + 2·48°, + 2·06°, and + 2·02°, in absolute ethyl alcohol, respectively, and melted at 158—159° (decomp.). The first fraction was recrystallised from alcohol 7 times and then had $[\alpha]_{5791}^{20^\circ}$ + 2·45° (Found : C, 40·9; H, 3·6. $C_{16}H_{15}O_7NTe$ requires C, 41·7; H, 3·3%). This crop gave rise to an inactive specimen of 2-aminophenoxtellurine, as did two other crops obtained during further fractionation. In all, 14 crops were examined polarimetrically and showed no difference in rotation except when they were obtained from concentrated mother-liquors and were dark in colour. Such crops had $[\alpha]_{5791}^{20^\circ}$ as high as + 3·15°, but no significance is attached to this slightly higher figure.

*2-Aminophenoxtellurine* d-*Camphorsulphonate*.—Equivalent solutions of the base (15·5 g.) and acid (11·6 g.) in hot alcohol were mixed (total volume, 400 c.c.). On cooling, rosettes of pale yellow needles, m. p. 182—185° (decomp.), separated (8·1 g.). By successive concentrations of the mother-liquor, 14·5 g. and 1·7 g. of salt were obtained. A fourth crop was too highly coloured for polarimetric examination, but the first three crops had $[\alpha]_{5791}^{20^\circ}$ + 14·0°, + 14·4°, and + 15·6°, respectively, in absolute ethyl alcohol. The third fraction, treated with ammonia, gave inactive base. The first fraction was recrystallised from aqueous acetone and gave 2 crops with $[\alpha]_{5791}^{20^\circ}$ + 15·3° and + 14·3°, a further crystallisation of the first of these crops leading to $[\alpha]_{5791}^{20^\circ}$ + 15·0° (Found : C, 46·7; H, 4·8. $C_{22}H_{25}O_5NSTe$ requires C, 48·6; H, 4·6%).

*2-Chloro-8-methylphenoxtellurine*.—4-Nitro-4'-methyldiphenyl ether, prepared from *p*-chloronitrobenzene and *p*-cresol by the usual method, was reduced with iron and acidified water at 100°, and the 4-amino-ether converted (65% yield) by the Sandmeyer process into 4-chloro-4'-methyldiphenyl ether (b. p. 168°/14 mm.; leaflets, m. p. 54°, from alcohol). Condensation of the chloro-ether with tellurium tetrachloride at 200°, or at 200—250°, gave very poor yields of 2-chloro-8-methylphenoxtellurine 10 : 10-dichloride. This was most conveniently prepared by heating 22 g. of the ether with 27 g. of tellurium tetrachloride for 3 hours at 160° and then for 8 hours at 200—240°. The brittle, dark red mass obtained on cooling was powdered, and extracted with ether until free from chloro-ether. The residue (40 g.) was crystallised from chloroform, in which much of it was insoluble. Tellurium (12 g.) was also isolated. In this way, 6 g. of reddish-brown microcrystalline dichloride, m. p. 284°, were obtained, and this was moistened with acetone and reduced with potassium anhydrosulphite and water. The resulting brown powder, when crystallised from alcohol, gave *2-chloro-8-methylphenoxtellurine* as yellow needles, m. p. 67—68° (Found : C, 45·4; H, 2·7. $C_{13}H_9OClTe$ requires C, 45·3; H, 2·6%).

*2-Chloromercuri-4'-methyldiphenyl Ether*.—The basis of the process used was the method of Nesmejanow (*loc. cit.*). 2-Amino-4'-methyldiphenyl ether (47 g.) was diazotised in hydrochloric acid with 14 g. of sodium nitrite, and the concentrated solution added, with stirring, to a solution of 54 g. of mercuric chloride in 54 c.c. of concentrated hydrochloric acid, to which 50 g. of ice had been added. The pale yellow crystalline precipitate of the diazomercuric chloride was filtered off, washed successively with water, alcohol, and ether, and then dried in the air. It was suspended in 400 c.c. of pure acetone at − 60°, and treated with copper powder freshly prepared from 120 g. of copper sulphate crystals and 26 g. of zinc dust. The rate of decomposition regulated the yield, which was highest when the reaction mixture was kept at − 60° for 12 hours, and then allowed slowly to attain the ordinary temperature during another 12 hours. The mixture was then filtered, and the residue extracted with hot acetone. The combined acetone extracts were concentrated to 200 c.c., and, on cooling, the *chloromercuri*-compound separated in stout needles. It was recrystallised from alcohol and then formed long, white, feathery needles, m. p. 140° (yield, 48 g.; 57%). It distils unchanged at 250—255°/15 mm. (Found : Hg, 47·7; Cl, 8·5. $C_{13}H_{11}OClHg$ requires Hg, 47·8; Cl, 8·5%).

*4'-Methyldiphenyl Ether 2-Telluritrichloride*.—To a solution of 41·9 g. of the mercurichloride in 300 c.c. of dry chloroform, 26 g. of tellurium tetrachloride (*i.e.*, slightly less than the calculated quantity) were added, and the whole was boiled under reflux for 1·5 hours. On cooling, mercuric chloride separated and was filtered off (25 g.). The filtrate was concentrated to 70 c.c., and, when kept, deposited 33 g. of the almost pure *telluritrichloride*, which was recrystallised from chloroform and obtained in massive yellow prisms or octahedra, m. p. 180—185° (decomp.) (yield, 80%) (Found : C, 36·3; H, 2·7. $C_{13}H_{11}OCl_3Te$ requires C, 37·1; H, 2·6%).

*2-Methylphenoxtellurine* 10 : 10-*Dichloride*.—The trichloride (16·8 g.) was heated for 0·5 hour in a large test-tube in a bath at 200—240°, with continual stirring. The deep red solid obtained on cooling was ground, and crystallised from acetone. The *dichloride* separated in pale yellow plates, m. p. 274—275° (12·2 g.; 80% yield) (Found: C, 41·5; H, 2·7. $C_{13}H_{10}OCl_2Te$ requires C, 41·0; H, 2·6%). A little tellurium was always formed.

2-*Methylphenoxtellurine*.—The dichloride was slowly reduced by potassium anhydrosulphite in presence of water, the mixture being ground at intervals during 24 hours. 2-*Methylphenoxtellurine* was then obtained in 93% yield. It tended to separate as an oil from solutions in light petroleum, but addition of a little alcohol prevented oil-formation and gave rosettes of needles, m. p. 50—52° (Found: C, 51·7; H, 3·55. $C_{13}H_{10}OTe$ requires C, 50·4; H, 3·2%). The 2-methylphenoxtellurine could not be oxidised with neutral or alkaline permanganate, or with chromic and acetic acids. The bulk of the material was destroyed and only small quantities of the telluroxide carboxylic acid were formed. Oxidation of the tellurine to the tellurone by means of hydrogen peroxide in acetone solution, followed by oxidation as above, also gave poor yields.

2-*Amino-4'-carboxydiphenyl Ether*.—2-Nitro-4'-methyldiphenyl ether was reduced to the amino-ether by the wet iron method, the base acetylated, and the 2-acetamido-4'-methyldiphenyl ether oxidised with neutral permanganate (Thompson and Turner, *loc. cit.*).

2-*Chloromercuri-4'-carboxydiphenyl Ether*.—The hydrochloride of 2-amino-4'-carboxydiphenyl ether (53 g.) was diazotised in hydrochloric acid, the final volume being about 350 c.c. The diazonium salt always crystallised ont, and in order to keep the solution as concentrated as possible, it was filtered off and redissolved in the least quantity of ice-cold water, in which it is considerably more soluble than in the dilute acid from which it separated. The solution was brought into reaction with mercuric chloride exactly as above, and the resulting pale yellow, microcrystalline diazomercuric chloride treated as before. It was suspended in 350 c.c. of pure acetone at − 60° (some of the salt dissolved) and treated with copper powder (2 atoms). The evolution of nitrogen started very briskly, but the yield of chloromercuri-compound reached a maximum when the reaction was allowed to take 48 hours. The mixture was then filtered, and the solid residue extracted several times with 100 c.c. portions of boiling acetone. The acetone was partly removed from the extract, and the chloromercuri-compound allowed to crystallise from about 200 c.c. of solution. It retained a greenish colour even after several crystallisations from acetone or alcohol, and the trace of copper responsible for this was removed by dissolving the product in sodium hydrogen carbonate solution and reprecipitating it with hydrochloric acid. The *chloromercuri*-compound then separated from alcohol in slender, pale buff-coloured needles, m. p. 220° (decomp.) (Found: Hg, 44·0; Cl, 8·1. $C_{13}H_9O_3ClHg$ requires Hg, 44·6; Cl, 7·9%).

4'-*Carboxydiphenyl Ether 2-Telluritrichloride*.—Interaction between the chloromercuri-compound and tellurium tetrachloride did not take place in boiling chloroform, benzene, or toluene, probably owing to the insolubility of the mercury derivative. Acetonitrile or dioxan can be used as solvent, but the former is more suitable in view of the extreme solubility of the product in dioxan.

The chloromercuri-compound (22·5 g.) was dissolved in 350 c.c. of hot acetonitrile, and 13 g. of tellurium tetrachloride (slightly less than the calculated qnantity) added. A deep red colour was immediately produced, and though this became less intense as the reaction proceeded, after 4 or 5 hours' boiling under reflux the solution was still highly coloured. The acetonitrile was partly distilled off, and the product allowed to crystallise from about 80 c.c. of solution. The mercuric chloride remained in the mother-liquor. The trichloride is almost insoluble in most non-hydroxylic solvents, but crystallises from acetonitrile in very small prisms, m. p. 205—206° (decomp.) (Found: C, 35·55; H, 2·4. $C_{13}H_9O_3TeCl_3$ requires C, 34·9; H, 2·0%).

2-*Carboxyphenoxtellurine* 10 : 10-*Dichloride*.—The trichloride was heated for 0·5 hour at 220—240°. Hydrogen chloride was evolved vigorously, and the colour gradually changed from dark red to greyish-brown. The mass was allowed to cool, powdered, and crystallised from acetone. A 62% yield of the pure *dichloride* was obtained, as white leaflets, m. p. 319° (Found: C, 38·0; H, 2·0. $C_{13}H_8O_3TeCl_2$ requires C, 38·0; H, 1·95%).

*Phenoxtellurine-2-carboxylic Acid*.—The dichloride (20·5 g.) was dissolved in a solution of 20 g. of sodium carbonate in 300 c.c. of water; the filtered solution was cooled to 0°, and reduced with 25 g. of potassium anhydrosulphite dissolved in the minimum of water. The colour changed from pale brown to a vivid yellow, and plates of the sodium salt of the reduced acid separated. Reduction at the ordinary temperature gave a dark product. The reaction

mixture was finally warmed to 40°, in order to dissolve the sodium salt, and the *acid* was precipitated with acetic acid. Mineral acids can only be used for the precipitation when there is a large excess of anhydrosulphite present, for otherwise the deep blue colour of tellurylium salts immediately appears. The acid was crystallised from alcohol or acetone. It forms heavy, bright yellow prisms, m. p. 231—233° (Found : C, 46·0; H, 2·7. $C_{13}H_8O_3Te$ requires C, 45·9; H, 2·4%).

*Decarboxylation of Phenoxtellurine-2-carboxylic Acid.*—A solution of 1 g. of the acid in 30 c.c. of dry quinoline was boiled for an hour in presence of a little copper-bronze. The cooled mixture was poured into dilute acetic acid. The crystalline deposit which was soon formed was removed, washed with dilute acetic acid and with water, and extracted with sodium carbonate solution. From the alkaline solution, 0·5 g. of unchanged acid was recovered, and by crystallising the alkali-insoluble material twice from light petroleum, 0·2 g. of phenoxtellurine was obtained. It melted at 77—79°, either alone or when mixed with pure phenoxtellurine.

*Experiments on the Resolution of Phenoxtellurine-2-carboxylic Acid.*—(a) *Nor-*d-ψ-*ephedrine salt.* A hot solution of 13·3 g. of nor-*d*-ψ-ephedrine in 50% aqueous alcohol was added to a suspension of 30 g. of the acid in the same hot solvent. The filtered solution obtained (550 c.c.) deposited pale yellow, flat needles (49 g.) of the *trihydrate* of the salt. Vacuum desiccation raised the m. p. from 76—80° to 130—140°, and further drying at 100° to 144—145° (Found : loss, 9·7 g. $C_{22}H_{21}O_4NTe,3H_2O$ requires $3H_2O$, 9·9 g. Found in *anhydrous* salt: C, 53·6; H, 4·7. $C_{22}H_{21}O_4NTe$ requires C, 53·8; H, 4·3%). The salt was very soluble in all solvents except light petroleum, and was therefore crystallised from aqueous alcohol and air-dried to the trihydrate. Two crops obtained during the preparation of the salt had $[\alpha]_{5791}^{20°}$ + 16·8° and + 16·9° in absolute ethyl alcohol. The first crop was recrystallised from aqueous alcohol 4 times : the rotation was then + 16·8°. Acid recovered from the last fraction was inactive. The mother-liquors were worked up and gave crops with rotations between + 16·7° and + 17·0°. In all, 16 crops were examined polarimetrically ($l$ = 2; $c$ = 2·5).

(b) *Strychnine salt.* The acid (16·98 g.) and strychnine (16·7 g.) were dissolved separately in absolute alcohol and the hot solutions mixed (1000 c.c.). The salt which separated on cooling in an ice chest was not crystalline and was solvated, but crystallisation at the ordinary temperature gave rosettes of needles, m. p. 198—200° (decomp.) (Found : C, 60·6; H, 4·6. $C_{34}H_{30}O_5N_2Te$ requires C, 60·6; H, 4·5%). The *salt* could only be crystallised from ethyl alcohol. Four crops obtained during the preparation were examined. The first (13·5 g.) after being crystallised 6 times changed in $[\alpha]_{5791}^{20°}$ only from − 14·5° to − 17·2°; the second (7·5 g.) from − 14·4° to − 15·9°; the third (9·0 g.) from − 14·6° to − 15·3° (in chloroform) during 2 crystallisations. Such crops as were decomposed gave inactive acid. The higher rotations were found to be due to separation of free strychnine together with the salt.

(c) *Quinine salt.* The acid (10·2 g.) and quinine (9·72 g.) were dissolved separately in hot alcohol and the solutions mixed. The *salt* separated in rosettes of hard glistening needles, m. p. 211° (Found : C, 59·5; H, 4·9. $C_{33}H_{32}O_5N_2Te$ requires C, 59·7; H, 4·8%). The three crops obtained weighed 16·0, 2·25, and 0·8 g. and had respectively $[\alpha]_{5791}^{20°}$ − 119·4°, − 122·3°, and − 121·6° in chloroform. After 3 recrystallisations from absolute alcohol the first crop had $[\alpha]_{5791}^{20°}$ − 125·1°. The acid liberated from it was inactive. The rotations of 12 crops were determined, and ranged from − 114° to − 126°, low figures being associated with partial decomposition of the salt in presence of light.

(d) *Cinchonidine salt.* Hot alcoholic solutions of 14·7 g. of cinchonidine and 16·9 g. of acid were mixed. From 500 c.c. of solution 17·8 g. of needles separated with m. p. 206° and $[\alpha]_{5791}^{20°}$ − 59·4° (Found : C, 60·2; H, 5·0. $C_{32}H_{30}O_4N_2Te$ requires C, 60·6; H, 4·7%). A second fraction of 4 g. had $[\alpha]_{5791}^{20°}$ − 59·1°. Recrystallisation of the first crop gave three fractions with $[\alpha]_{5791}^{20°}$ − 58·9°, − 57·9°, and − 57·8°. In all, eight crops were examined, and several were decomposed, giving inactive acid.

(e) d-α-*Phenylethylamine salt.* When a hot solution of 6·05 g. of base in 50 c.c. of alcohol was added to one of 16·98 g. of acid in 400 c.c. of alcohol, salt separated, and was redissolved after adding 150 c.c. of alcohol. Four fractions of salt separated in turn. These weighed 12·5, 4·5, 2·5, and 2 g., and had $[\alpha]_{5791}^{20°}$ + 3·97°, + 4·19°, + 3·90°, and + 3·85°, respectively. The first fraction was recrystallised twice from alcohol and then had m. p. 205° and $[\alpha]_{5791}^{20°}$ + 4·05°. Three further crystallisations from methyl alcohol gave 1·8 g. with $[\alpha]_{5791}^{20°}$ + 3·88°. Inactive acid was obtained from more than one crop. The original second and third fractions were together crystallised from acetone, giving $[\alpha]_{5791}^{20°}$ + 4·09°, and the new crop was then crystallised from methyl alcohol, the rotation finally being + 4·04°. The rotations of 11

crops of different origins were actually determined, and ranged from + 3·80° to + 4·19° ($l$ = 2; $c$ = 1; methyl alcohol) (Found: C, 54·6; H, 4·2. $C_{22}H_{21}O_3NTe$ requires C, 54·7; H, 4·1%).

*Partial Esterification of Phenoxtellurinecarboxylic Acid with* l-*Menthol*.—The acid (3·4 g.) and *l*-menthol (5 g.) were heated together under reflux for 7—8 hours. The whole was dissolved in ether, and the ethereal solution extracted with sodium carbonate solution, from which 1·0 g. of acid was subsequently recovered. The ethereal solution was steam-distilled, and when the product was free from menthol it was crystallised from alcohol. The l-*menthyl ester* was so obtained as yellow prisms, m. p. 123—125°. It was recrystallised twice from alcohol and once from acetone, but the crops varied in $[\alpha]_{5791}^{20°}$ only from − 51·9° to − 52·2° in acetone (Found: C, 57·6; H, 5·6. $C_{23}H_{26}O_3Te$ requires C, 57·8; H, 5·5%).

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# 11. *Studies on the Michael Reaction. Part II. The Nature of the Condensation Product from Ethyl Benzylmalonate and Ethyl Fumarate.*

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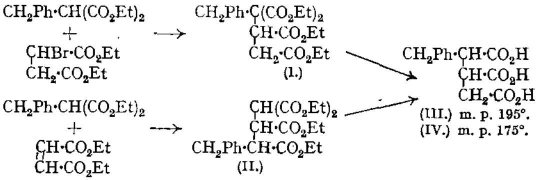
In agreement with Malachowski *et al.* (*Ber.*, 1936, 69, 1295), the product of this condensation gives rise, on acid hydrolysis, to a mixture of stereoisomeric α-benzyltricarballylic acids which are mutually interconvertible under the conditions of hydrolysis. Nevertheless, the product is structurally different from that obtained by condensation of ethyl benzylmalonate with ethyl α-bromosuccinate, since the proportions of the stereoisomeric acids obtained on hydrolysis differ in the two cases.

THE work here described was carried out in an endeavour to explain the divergence between the results of Malachowski, Bilbel, and Belinski-Tarasowicz (*Ber.*, 1936, 69, 1295) and those of the earlier workers (Duff and Ingold, J., 1934, 87; Rydon, J., 1935, 420). Whereas both Duff and Ingold and Rydon isolated different, stereoisomeric α-benzyltricarballylic acids (III) and (IV) from the condensation products, (I) and (II), of ethyl benzylmalonate with ethyl α-bromosuccinate and with ethyl fumarate respectively, Malachowski and his co-workers claimed to have shown that both esters gave the same mixture of stereoisomerides on acid hydrolysis; on these grounds they questioned the difference in structure of the esters (I) and (II).




Repetition of the condensations with carefully purified materials gave two esters which differed markedly in physical properties:

| | B. p. | $n_D^{17·8°}$. | $d_{4°}^{17·3°}$. | $[R_L]_D$. Found. | $[R_L]_D$. Calc. |
|---|---|---|---|---|---|
| Ester (I) ................. | 205—207°/1·3 mm. | 1·4880 | 1·1351 | 107·11 | 106·81 |
| Ester (II) ................. | 198—200°/0·9 mm. | 1·4841 | 1·1287 | 106·75 | 106·81 |

Malachowski and his co-workers found that acid hydrolysis, under certain conditions, brought about interconversion of the stereoisomeric α-benzyltricarballylic acids (III) and

(IV). Accordingly the two esters were hydrolysed under a variety of conditions, and the products submitted to careful fractional crystallisation. With the aid of a melting-point curve obtained with synthetic mixtures of the acids it was possible to make a close estimate of the proportion of the two acids obtained in each experiment.

The four methods of hydrolysis used were: (a) Seventy hours' refluxing with three volumes of 20% hydrochloric acid. (b) Five hours' refluxing with ten volumes of Malachowski's formic–sulphuric acid mixture [one volume of water, three volumes of concentrated sulphuric acid, nine volumes of formic acid; this mixture is more concentrated than that used by Duff and Ingold and by Rydon; see (d)]. (c) Forty hours' refluxing with Malachowski's mixture. (d) Twenty hours' refluxing with one volume of water, one volume of concentrated sulphuric acid, and three volumes of formic acid.

The results of the fractional crystallisations were:

| Method of hydrolysis. | Ester (I). % (III). | Ester (I). % (IV). | Ester (II). % (III). | Ester (II). % (IV). |
|---|---|---|---|---|
| (a) | 53 | 47 | 42 | 58 |
| (b) | 51 | 49 | 35 | 65 |
| (c) | 85 | 15 | 55 | 45 |
| (d) | 61 | 39 | 51 | 49 |

These results confirm Malachowski's observation that a stereo-conversion in the sense (IV) ⟶ (III) occurs during the acid hydrolysis; they also show clearly, however, that in every case more of the acid (III) is obtained from the ester (I) than from the ester (II). Both Duff and Ingold (*loc. cit.*) and Rydon (*loc. cit.*) isolated only the acid (III) from the ester (I) and the acid (IV) from the ester (II), using essentially method (d) for hydrolysis; control experiments showed that the solubility relationships are such that, without recourse to careful fractional crystallisation, the mixtures obtained by method (d) do indeed behave in this manner, the product from (I) giving a pure specimen of (III) and the product from (II) a pure specimen of (IV) as the first individual acids to be isolated.

It was, further, found that treatment of the ester (I) with sodium ethoxide gave rise to a product which, on hydrolysis by method (b), yielded 37% of the acid (III) and 63% of (IV); this proportion closely corresponds with that obtained from the ester (II) by this method of hydrolysis and indicates the conversion of (I) into (II) by the sodium ethoxide.

On the basis of these experiments we adhere to the view that the esters (I) and (II) are indeed structurally different, at any rate so far as the principal constituent of each is concerned. Malachowski's statement that the differences shown by the two esters on attempted methylation [(II) can be methylated, whereas (I) cannot (Rydon, *loc. cit.*)] are "nicht grösser als man sie bei Präparaten derselben Substanz von verschiedenem Reinheitsgrad finden könnte" cannot be accepted.

## EXPERIMENTAL.

*Ethyl Benzylmalonate.*—The bulk of the material used was prepared by the method of Leuchs (*Ber.*, 1911, **44**, 1509) and had b. p. 150—152°/4 mm. A specially pure ester was prepared by hydrolysing this to the acid, which was recrystallised from benzene–light petroleum; 20 g. of this acid, m. p. 121°, were refluxed for 24 hours with 75 c.c. of alcohol, 110 c.c. of benzene, and 12 c.c. of concentrated sulphuric acid. The solution was poured into water, and an ethereal extract washed with 10% sodium carbonate solution and water; distillation of the dried extract gave 22 g. (85%) of pure ethyl benzylmalonate, b. p. 140—140·5°/1·5 mm.

*Condensation of Ethyl Benzylmalonate with Ethyl Bromosuccinate.*—125 G. of ethyl benzylmalonate were added to sodium ethoxide (from 11·5 g. of sodium and 160 c.c. of absolute alcohol). 127 G. of ethyl α-bromosuccinate (b. p. 136—138°/17 mm.) were then added to the cooled mixture, and the product refluxed overnight. The product was poured into water, acidified with dilute sulphuric acid, and extracted with ether. Distillation of the dried extract, after washing with 10% sodium carbonate solution and water, yielded 113 g. of a fraction, b. p. 218—224°/3 mm. Redistillation gave 105 g. of ethyl δ-phenyl-*n*-butane-αβγγ-tetracarboxylate (I), b. p. 214—216°/2 mm., as a pale yellow oil with a slight green

fluorescence. A very pure specimen obtained similarly from ethyl benzylmalonate prepared from the acid had b. p. 205—207°/1·3 mm., $n_D^{17\cdot3°}$ 1·4880, $d_{4°}^{17\cdot3°}$ 1·1351, $[R_L]_D$ 107·11 (calc., 106·81) (Malachowski, Bilbel, and Belinski-Tarasowicz, *loc. cit.*, give b. p. 206—208°/1·5 mm., $n_D^{20°}$ 1·4862, $d_{4°}^{20°}$ 1·1338).

*Hydrolysis.* Hydrolysis was carried out by refluxing with the appropriate reagent for a definite time; the product crystallising on cooling was then recrystallised once from 20% hydrochloric acid (except when this was used for the hydrolysis) in order to remove sulphuric acid. The crude acid so obtained was systematically fractionally crystallised from glacial acetic acid, the minimum amount of solvent being used in the first crystallisation and thereafter 3 parts by weight. The composition of fractions too small for further crystallisation was determined by reference to a melting-point curve constructed from the following data on synthetic mixtures of the two α-benzyltricarballylic acids, m. p. 195° (III) and m. p. 175° (IV):

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| % (III) ...... | 0 | 10 | 20 | 27 | 40 | 50 | 60 | 67·5 | 75 | 80 | 100 |
| M. p. ......... | 175° | 169° | 166° | 165° | 166° | 167·5° | 169° | 171° | 173° | 174·5° | 195° |

Four hydrolyses were carried out: (a) 5·5 G. with 30 c.c. of 20% hydrochloric acid; 67 hours. Crude product: 3·08 g. (90%), m. p. 167—171°. Recrystallisation gave 1·00 g. of (IV), m. p. 175°, 1·00 g. of an acid, m. p. 188—190°, 97·5% of (III), and 0·30 g. of an acid, m. p. 170—174°, 78·5% of (III). Hence, based on recrystallised material, the product contained 53% of (III) and 47% of (IV); recovery, 75%.

(b) 5 G. with 50 c.c. of Malachowski's mixture (see p. 43); 5 hours. Crude product: 2·70 g. (86%), m. p. 155—159°. This gave 0·80 g. of (IV), m. p. 174—175°; 0·60 g., m. p. 189—192°, 99% of (III); 0·30 g., m. p. 167—169°, 58% of (III); 0·20 g., m. p. 180—183°, 93% of (III). Hence, 51% of (III) and 49% of (IV); recovery, 70%.

(c) 5·4 G., as (b); 37 hours. Crude product: 3·20 g. (92%), m. p. 160—168°. This gave 1·30 g., m. p. 188—191°, 98% of (III); 0·30 g., m. p. 172—176°, 83% of (III); 0·45 g., m. p. 166—170°, 63% of (III); 0·15 g., m. p. 164—167°, 47% of (III). Hence 85% of (III) and 15% of (IV); recovery, 69%.

(d) 5·3 G. with 5 c.c. of water, 5 c.c. of sulphuric acid, and 15 c.c. of formic acid; 20 hours. Crude product: 3·00 g. (90%), m. p. 150—160°. This gave 1·10 g., m. p. 190—192°, 99% of (III); 0·40 g., m. p. 173—174°, 1% of (III); 0·10 g., m. p. 181—185°, 94% of (III); 0·40 g., m. p. 168—170°, 9% of (III). Hence 61% of (III) and 39% of (IV); recovery, 67%.

*Action of sodium ethoxide.* 15·5 G. of the ester (I) were added to sodium ethoxide (from 0·75 g. of sodium and 12 c.c. of absolute alcohol), and the mixture refluxed for 48 hours. The product was poured into water and extracted with ether, and the extract washed with 10% sodium carbonate solution and water, dried, and distilled. Three fractions were collected at 3 mm.: (1) b. p. 140—160°, 3·0 g.; (2) b. p. 160—215°, 1·3 g.; (3) b. p. 215—220°, 2·1 g. Fraction (1) was identified as ethyl benzylmalonate by hydrolysis to the acid (mixed m. p.). Fraction (3) was boiled with 20 c.c. of Malachowski's mixture for 5 hours and gave 0·9 g. of a crude acid, m. p. 156—158°. Fractional crystallisation gave 0·2 g., m. p. 184—186°, 95% of (III), and 0·5 g., m. p. 166—168°, 13% of (III). Hence, 37% of (III) and 63% of (IV); recovery, 78%.

*Condensation of Ethyl Fumarate and Ethyl Benzylmalonate.*—43 G. of ethyl fumarate and 56 g. of ethyl benzylmalonate were added to sodium ethoxide prepared from absolute alcohol (70 c.c.) and sodium (5·6 g.). After being left at room temperature for 14 days, the red solution was poured into water, acidified, and extracted with ether. The extract was washed with 10% sodium carbonate solution and water, dried, and distilled. Refractionation of the product (54 g.), b. p. 200—224°/3·5 mm., yielded 42 g. (42%) of the pure condensation product (II), b. p. 216—218°/2·5 mm., as a practically colourless oil with a very slight green fluorescence. A specimen, prepared similarly from ethyl benzylmalonate made from the specially purified acid, had b. p. 198—200°/0·9 mm., $n_D^{17\cdot3°}$ 1·4841, $d_{4°}^{17\cdot3°}$ 1·1287, $[R_L]_D$ 106·75 (calc., 106·81) (Malachowski *et al.*, *loc. cit.*, give b. p. 208—210°/1·5 mm., $n_D^{20°}$ 1·4851, $d_{4°}^{20°}$ 1·1283).

*Hydrolysis.* Four experiments were carried out: (a) 5·4 G. with 30 c.c. of 20% hydrochloric acid; 72 hours. Crude product: 3·15 g. (92%), m. p. 169—171°. This gave 0·90 g. of (IV), m. p. 175°; 0·50 g., m. p. 188—191°, 98% of (III); 0·30 g., m. p. 168—170°, 8·5% of (III); 0·80 g., m. p. 168—171°, 67% of (III). Hence 42% of (III) and 58% of (IV); recovery, 79%.

(b) 5·9 G. with 50 c.c. of Malachowski's mixture; 5 hours. Crude product: 3·05 g. (82%), m. p. 152—156°. This gave 0·80 g. of (IV), m. p. 175°; 0·50 g., m. p. 187—189°, 96% of

(III); 0·50 g., m. p. 169—172°, 5% of (III); 0·40 g., m. p. 168—171°, 68% of (III). Hence, 35% of (III) and 65% of (IV); recovery, 72%.

(c) As (b); 40 hours. Crude product: 2·70 g. (85%), m. p. 151—153°. This gave 0·90 g. of (III), m. p. 193—194°; 0·50 g. of (IV), m. p. 175°; 0·40 g., m. p. 164—166°, 21% of (III). Hence, 55% of (III) and 45% of (IV); recovery, 67%.

(d) 5 G. with 5 c.c. of water, 5 c.c. of sulphuric acid, and 15 c.c. of formic acid; 20 hours. Crude product: 2·60 g. (82%), m. p. 152—157°. This gave 0·50 g. of (IV), m. p. 175°; 0·20 g., m. p. 166—169°, 58% of (III); 0·30 g., m. p. 168—172°, 71% of (III); 0·50 g., m. p. 167—171°, 66% of (III); 0·25 g., m. p. 186—188°, 96% of (III). Hence, 51% of (III) and 49% of (IV); recovery, 68%.

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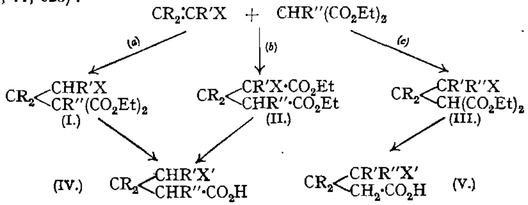
## 12. *Studies on the Michael Reaction. Part III. General Considerations: The Addition of Alkylmalonic Esters to Some Unsaturated Diketones.*

By J. A. GARDNER and H. N. RYDON.

Abnormal Michael reactions, *viz.*, those in which an apparent migration of an alkyl group occurs, can be explained on the basis of two different mechanisms. In Thorpe's mechanism the sodioalkylmalonic ester is held to split into alkyl and sodiomalonic residues during the addition, whereas according to Holden and Lapworth's mechanism the ester is believed to add normally as a sodium kation and an alkylmalonic ester anion, the abnormal product arising as a result of isomerisation of the primary normal product. It is shown, from general considerations, that experimental discrimination between these mechanisms is only possible when the unsaturated reactant is a ketone or an α-substituted ester. The condensation of ethyl benzylmalonate with dibenzoyl- and diacetyl-ethylenes is complicated by a side reaction, the nature of which is discussed; the condensation with dibenzoylethylene is shown to proceed normally under certain conditions.

THE products to be expected in the general case of the reaction between an alkylmalonic ester and a suitable unsaturated compound, according to the mechanism controlling the reaction, are set out in the following scheme, in which route (*a*) indicates the normal mechanism, route (*b*) the course of the reaction according to the mechanism of Holden and Lapworth (J., 1931, 2370), and route (*c*) the course required by Thorpe's mechanism (J., 1900, **77**, 923):



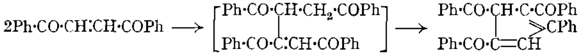

X is an activating group (such as $CO_2Et$, COR or CN), which passes into X' (*e.g.*, $CO_2H$, COR) on acid hydrolysis; (I), (II), and (III) are the expected condensation products, and (IV) and (V) the acids into which they pass on acid hydrolysis.

Inspection shows that routes (*a*) and (*b*) yield the same acid (IV). It is therefore evident that the corresponding mechanisms can only be differentiated by comparison of the condensation products (I) and (II) or the acids obtained from these by alkaline hydrolysis; such a comparison will also differentiate both of these routes from route (*c*). Such a comparison is, however, not always experimentally possible (cf. Part I, J., 1935,

420); for this reason, in a search for reactions proceeding by Thorpe's mechanis (route *c*), it is desirable so to choose the reactants that (IV) and (V) will be differen Now (IV) = (V) if R″ = H, hence substituted malonic esters must be used. With th proviso, (IV) and (V) are also identical if X′ = $CO_2H$ (X = $CO_2Et$ or CN) *and* R′ = H we may thus distinguish between (IV) and (V) only if either X′ ≠ $CO_2H$ (*i.e.*, X ≠ $CO_2$I or CN) or R′ ≠ H. That is to say, the most suitable reactions are those in which a alkylmalonic ester is added to an unsaturated ketone or to an α-substituted unsaturate ester. The present paper is concerned with the first class of reaction and Part I (following paper) with the second.

Since it had been shown (Parts I and II) that the condensation of ethyl benzylmalona with ethyl fumarate is abnormal (route *b* or *c*), it was decided to use ketonic analogues the latter of the type R·CO·CR:CR·COR. The first diketone to be studied wa αβ-dibenzoylethylene (VI), the *trans*-modification of which is readily accessible (Conan and Lutz, *J. Amer. Chem. Soc.*, 1923, **45**, 1303). The earlier experiments showed th Michael reaction with this substance to be complicated by a side reaction, which wa investigated.

At room temperature, dibenzoylethylene reacted with one equivalent of sodiu ethoxide in alcoholic solution to give, as the principal product, a bright orange substanc $C_{32}H_{22}O_3$, m. p. 161°. This substance, although unsaturated, was very resistant t catalytic hydrogenation, and only benzoic acid could be isolated on oxidation wit potassium permanganate. It is suggested that the reaction consists in an intermolecul condensation of two molecules of dibenzoylethylene (cf. ethyl crotonate; von Pechman *Ber.*, 1900, **33**, 3340), followed by the elimination of a molecule of water between th methylene group so formed and one carbonyl group, the orange material bei 1 : 4 : 5-*tribenzoyl*-2-*phenyl*cyclo*pentadiene* (VII or a tautomeride of this) :



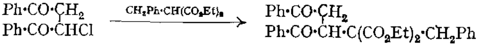
(VI.) (VII.)

αβ-Diacetylethylene (Armstrong and Robinson, J., 1934, 1650) formed tarry produc with sodium ethoxide; an attempt to condense this substance with ethyl sodiomalona gave a small amount of a ketonic oil, the semicarbazone of which furnished the analytic figures required for the monosemicarbazone of a product similar to (VII).

If the above view of the mechanism of this side reaction is correct, an unsaturat diketone without hydrogen atoms on the ethylenic carbons should be stable towar sodium ethoxide. Such a diketone is αβ-dibenzoylstilbene, Ph·CO·CPh:CPh·COPh, an in conformity with this view, it underwent no reaction on treatment with sodiu ethoxide.

Bearing in mind this remarkable reactivity towards sodium ethoxide, we ma experiments on the addition of ethyl benzylmalonate to *trans*-αβ-dibenzoylethyler Addition occurred rapidly and smoothly under the influence of alcoholic sodium ethoxi at — 20°; the product, m. p. 92°, was the expected addition compound.

The normal addition product was synthesised by condensation of α-chloro-α dibenzoylethane (VIII) (Paal and Schultze, *Ber.*, 1902, **35**, 171) with ethyl benzylmalonat

(VIII.)  (IX.)

*Ethyl* γδ-*dibenzoyl*-α-*phenylbutane*-ββ-*dicarboxylate* (IX), so obtained, had m. p. 9 unchanged on admixture with the condensation product from dibenzoylethylene a ethyl benzylmalonate; this addition, therefore, proceeds by route (*a*), *i.e.*, it is norm in mechanism.

All attempts to bring about the addition of ethyl benzylmalonate to *cis*-α dibenzoylstilbene were fruitless.

## Experimental.

*trans*-αβ-Dibenzoylethylene was prepared by the Friedel–Crafts reaction between fuma chloride and benzene (Conant and Lutz, *loc. cit.*).

*Action of Sodium Ethoxide on Dibenzoylethylene.*—2·5 G. of dibenzoylethylene were suspended in 50 c.c. of absolute alcohol, and sodium ethoxide [from sodium (0·25 g.) and absolute alcohol (10 c.c.)] added. The mixture immediately became deep red and the dibenzoylethylene dissolved. After 10 minutes the solution was poured into water; the buff-coloured precipitate, m. p. 65—68°, obtained was too intractable to allow of further study. Acidification of the deep red filtrate precipitated 1·5 g. of a dark red solid. Crystallisation from alcohol yielded bright orange needles, m. p. 161°, which were probably 1 : 4 : *5-tribenzoyl-2-phenyl*cyclo*pentadiene* (VII) [Found : C, 84·0, 83·9; H, 5·0, 4·7; *M* (Rast), 444. $C_{32}H_{22}O_3$ requires C, 84·6; H, 4·8%; *M*, 454]. No hydrogen was absorbed when 1·0 g. of this material was shaken with 0·2 g. of Adams's platinum catalyst, suspended in acetic acid or alcohol, in an atmosphere of hydrogen for 3 days. 2·8 G. of powdered potassium permanganate were added to a mechanically stirred ice-cold solution of 0·7 g. of the product in acetone; only benzoic acid (0·4 g.; 53%) was isolated.

When dibenzoylethylene was refluxed with sodium ethoxide for several hours, only resinous products were obtained.

*Addition of Ethyl Benzylmalonate to Dibenzoylethylene.*—5 G. of ethyl benzylmalonate were added to a solution of 0·46 g. of sodium in 10 c.c. of absolute alcohol, and the mixture refluxed for 10 minutes. It was then cooled in an ice–salt freezing mixture, and a cooled suspension of 4·8 g. of dibenzoylethylene in 10 c.c. of alcohol added slowly. After about 10 minutes all the dibenzoylethylene dissolved and a white solid was precipitated. The mixture was left overnight, and the precipitate filtered off and washed with alcohol. The crude material (2·5 g.) was crystallised from light petroleum (b. p. 40—60°), yielding 2·0 g. (20%) of *ethyl γδ-dibenzoyl-α-phenyl-*n*-butane-ββ-dicarboxylate* (IX) in clusters of prisms, m. p. 92°, mixed m. p. with the synthetic product (below) 92° (Found : C, 73·7; H, 6·0. $C_{30}H_{30}O_6$ requires C, 74·1; H, 6·2%).

*Condensation of α-Chlorodibenzoylethane with Ethyl Benzylmalonate.*—2·4 G. of pulverised sodium were suspended in dry ether, 25 g. of ethyl benzylmalonate added, and the solution refluxed until all the sodium had reacted. 27 G. of α-chlorodibenzoylethane (VIII) (Paal and Schultze, *loc. cit.*), suspended in ether, were added, and refluxing continued; the mixture was at first deep red, but the colour gradually lightened to a pale brown. The sodium chloride was removed, and the ethereal filtrate washed with water, dried over sodium sulphate, and evaporated. The viscous product deposited a solid, which was filtered off and washed with light petroleum. Three crystallisations of the crude yellow material (23 g.; 46%) from light petroleum (b. p. 60—80°) yielded ethyl γδ-dibenzoyl-α-phenyl-*n*-butane-ββ-dicarboxylate (IX) in clusters of colourless prismatic needles, m. p. 92° (Found : C, 73·6; H, 5·9%). A substance, m. p. 133°, was also obtained, but in amount too small to allow of further investigation.

*Ethyl Diacetylsuccinate.*—The following is an improvement of the method of Knorr (*Ber.*, 1894, **27**, 1155) and requires less solvent than the modification due to Bilton and Linstead (J., 1937, 924) : 250 G. of ethyl acetoacetate, dissolved in 250 c.c. of dry ether, were run slowly (cooling when necessary) into a mechanically stirred suspension of 46 g. of " molecular " sodium in 750 c.c. of dry ether. When all the sodium had reacted, an ethereal suspension of 200 g. of finely powdered iodine was added slowly with stirring. When no further decolorisation of the iodine was observed, the sodium iodide was filtered off and washed with dry ether. The ethereal filtrate was evaporated, and the residue crystallised from 50% acetic acid, yielding 110 g. (42%) of pure ethyl diacetylsuccinate, m. p. 89—90°.

The ester was converted by Knorr's method (*Ber.*, 1900, **33**, 1219) into acetonylacetone; this was dehydrogenated to diacetylethylene, m. p. 77—78°, following Armstrong and Robinson (*loc. cit.*).

*Attempted Condensation of Ethyl Malonate and Diacetylethylene.*—1·7 G. of diacetylethylene, dissolved in 10 c.c. of absolute alcohol, were added to ethyl sodiomalonate (sodium, 0·35 g.; absolute alcohol, 5 c.c.; ethyl malonate, 2·4 g.). The solution became red and then brown; it was refluxed overnight, poured into water, and acidified. Resinous material (0·7 g.) was filtered off, and the filtrate extracted with ether. Distillation of the dried extract yielded 0·6 g. of a high fraction, b. p. 113—117°/1·5 mm., which gave a *semicarbazone*, m. p. 186—187° (Found : N, 16·1. $C_{13}H_{17}O_3N_3$ requires N, 16·0%).

*Action of Sodium Ethoxide on Dibenzoylstilbene.*—2·0 G. of *cis*-dibenzoylstilbene (Nadelung and Oberwegner, *Annalen*, 1931, **490**, 234) were added to sodium ethoxide [from sodium (0·15 g.) and absolute alcohol (5 c.c.)], and the solution refluxed overnight. When it was poured into water, *cis*-dibenzoylstilbene was reprecipitated, m. p. (after recrystallisation) and mixed m. p. 214°.

*Attempted Addition of Ethyl Benzylmalonate to Dibenzoylstilbene.*—2·5 G. of ethyl benzyl-

malonate were added to sodium ethoxide (from 0·23 g. of sodium and 10 c.c. of absolut alcohol). A suspension of 3·8 g. of dibenzoylstilbene in absolute alcohol was added, and th mixture kept overnight. The dibenzoylstilbene remaining undissolved, the mixture wa refluxed for 48 hours on the steam-bath. On cooling, a solid was precipitated (3·7 g.), m. p 210—213°. Recrystallisation showed this to be unchanged *cis*-dibenzoylstilbene, m. p. an mixed m. p. 214°.

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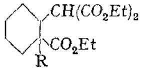
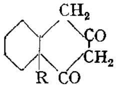
## 13. *Studies on the Michael Reaction. Part IV. The Addition c Alkylmalonic Esters to Some α-Substituted $\Delta^{\alpha}$-Unsaturated Esters General Conclusions.*

By J. A. GARDNER and H. N. RYDON.

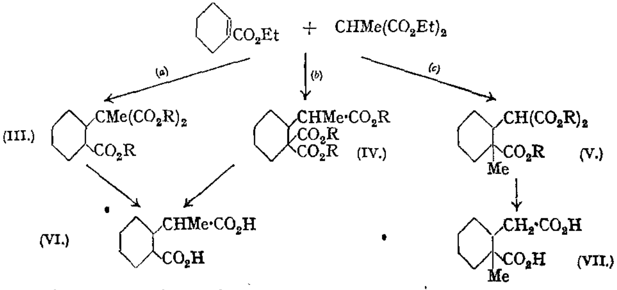
The condensations of ethyl methylmalonate with ethyl $\Delta^1$-tetrahydrobenzoate and with ethyl α-ethylcrotonate and of ethyl ethylmalonate with ethyl tiglate have been studied. Comparison of the products with synthetic materials shows that in every case the reaction proceeds normally, *i.e.*, without apparent wandering of alkyl or carbethoxyl. The results of Parts I—IV and of other workers are correlated and are all shown to be in accordance with predictions based on Holden and Lapworth's theory of abnormal reactions. It is concluded that, although no direct proof has been obtained, this agreement of theory and practice points strongly to the validity of Holden and Lapworth's views.

THE addition of alkylmalonic esters to ethyl $\Delta^1$-tetrahydrobenzoate is of great interest the present time, since, if it could be established that such additions are abnormal a proceed by route (*c*),* yielding (I), an obvious extension, using acetoacetic esters and Δ

(I.)   (II.)

tetrahydroacetophenone, should give rise to substances of type (II), by ring closure aft the manner of Vorländer's well-known synthesis of dimethyldihydroresorcinol (*Annal* 1897, **294**, 314).

The products to be expected, according to the prevailing mechanism, in the condensati of ethyl methylmalonate with ethyl $\Delta^1$-tetrahydrobenzoate are shown in the followi scheme:




* In this paper the various mechanisms are distinguished as routes (*a*), (*b*) and (*c*) as in Part (J., 45).

in which, when R = Et, (III), (IV) and (V) represent the reaction products and, when R = H, the tribasic acids obtainable therefrom by alkaline hydrolysis, and (VI) and (VII) represent the dibasic acids to be expected on acid hydrolysis. Of the esters (III), (IV) and (V), only the last should be capable of ready alkylation.

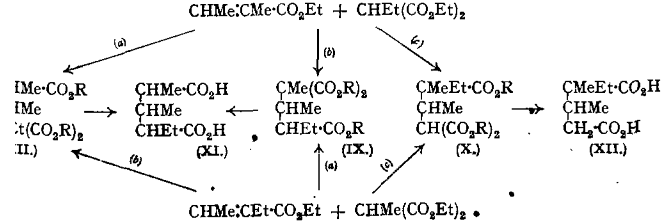
Of these products, the two forms of 1-methyl*cyclo*hexane-1-carboxylic-2-acetic acid (VII) are known. The *cis*(?)-acid, m. p. 163—164°, was prepared by the method of Linstead and Millidge (J., 1936, 840; cf. Chuang, Tien, and Huang, *Ber.*, 1935, **68**, 864), and the *trans*(?)-acid, m. p. 174° (Linstead and Millidge, *loc. cit.*; Newitt, Linstead, Sapiro, and Boorman, J., 1937, 879), was kindly supplied by Dr. Linstead.

The "normal" addition product (III; R = Et) was synthesised by condensing ethyl $\Delta^1$-tetrahydrobenzoate with ethyl sodiomalonate (cf. Helfer, *Helv. Chim. Acta*, 1926, **9**, 816; Boorman and Linstead, J., 1935, 258) and methylating the product in the usual way. Alkaline hydrolysis of ethyl *cyclo*hexane-1-carboxylate-2-methylmalonate (III; R = Et) so obtained could not be made to yield any of the desired tribasic acid (III; R = H) owing to extensive decarboxylation, but acid hydrolysis readily yielded cyclo*hexane*-1-*carboxylic*-2-α-*propionic acid* (VI), m. p. 184°. Since Boorman and Linstead (*loc. cit.*) showed that the parent unmethylated ester gave only *trans*-hexahydrohomophthalic acid on acid hydrolysis, the disposition of the groups about the ring is probably *trans*; the stereochemical arrangement with respect to the methyl group is uncertain, but evidence was obtained of change on heating with hydrochloric acid at 190°, indicating that the acid may have the *trans-cis*-configuration.

The addition of ethyl methylmalonate to ethyl $\Delta^1$-tetrahydrobenzoate under the influence of one equivalent of sodium ethoxide was very incomplete; after many trials the best yield (6%) was obtained by heating the reactants together on the steam-bath for 56 hours. This disappointing yield is in marked contrast to the 46% yield obtained by using ethyl malonate and the reaction affords an extreme example of the reduced tendency to addition caused by alkylation of the malonic ester (cf. Cooper, Ingold, and Ingold, J., 1926, 1868). The product had physical properties ($d_4^{20°}$ 1·080, $n_D^{20°}$ 1·463) which were very close to those ($d_4^{20°}$ 1·079, $n_D^{20°}$ 1·463) of the synthetic ester (III; R = Et) (values corrected to 20°). Alkaline hydrolysis gave no tribasic acid but only a dibasic acid, m. p. 184°, which was identified as *cyclo*hexane-1-carboxylic-2-α-propionic acid (VI) by a mixed m. p. termination with the synthetic specimen. Attempted methylation of the condensation oduct, using "molecular" sodium in benzene, gave considerable amounts of retrogression oducts, one of which was identified as ethyl dimethylmalonate, but no methylated aterial.

The identification of the dibasic acid and the failure of the attempted methylation early exclude route (*c*); the very close approximation of the physical constants for the nthetic ester (III; R = Et) and the condensation product is strong evidence in favour route (*a*), as is the identification of ethyl dimethylmalonate among the retrogression oducts from the attempted methylation. We are thus led to conclude that in this retion the normal mode of addition [route (*a*)] prevails.

The additions of ethyl ethylmalonate to ethyl tiglate and of ethyl methylmalonate to hyl α-ethylcrotonate were studied together, since the expected products are closely ated:



Of the acids required for reference, (XI) and (IX; R = H) were synthesised. Condensation of ethyl tiglate and ethyl malonate, under the influence of cold alcoholic sodium ethoxide for 14 days, gave a 60% yield of ethyl γ-carbethoxy-αβ-dimethylglutarate; Michael and Ross (*J. Amer. Chem. Soc.*, 1930, **52**, 4602), using ethereal sodium ethoxide, record a yield of only 15%. Ethylation of this product in benzene yielded *ethyl γ-carbethoxy-αβ-dimethyl-γ-ethylglutarate* (VIII; R = Et); neither alkaline nor acid hydrolysis gave crystalline products.

Ethyl α-ethylcrotonate readily condensed with ethyl malonate, under the influence of alcoholic sodium ethoxide, to yield *ethyl α-carbethoxy-β-methyl-γ-ethylglutarate*, which was methylated in benzene solution to *ethyl α-carbethoxy-αβ-dimethyl-γ-ethylglutarate* (IX; R = Et). Alkaline hydrolysis of the latter yielded *α-carboxy-αβ-dimethyl-γ-ethylglutaric acid* (IX; R = H) as a solid, m. p. 161°; acid hydrolysis gave a semi-solid product, from which one of the stereoisomeric *αβ-dimethyl-γ-ethylglutaric acids* (XI), m. p. 123°, was readily isolated.

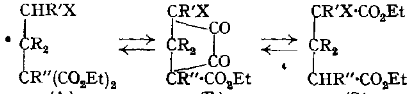
The formation of different stereoisomerides, or mixtures of stereoisomerides, from the esters (VIII; R = Et) and (IX; R = Et) is not without precedent; thus, in the analogous and stereochemically less complicated case of the methylethylcarboxysuccinic esters, Bischoff and Mintz (*Ber.*, 1890, **23**, 647) showed that, whereas the ester $CO_2Et{\cdot}CHEt{\cdot}CMe(CO_2Et)_2$ gave a mixture of *cis-* and *trans*-methylethylsuccinic acids on acid hydrolysis, the ester $CO_2Et{\cdot}CHMe{\cdot}CEt(CO_2Et)_2$ gave only the *trans*-acid.

The yield in the condensation of ethyl ethylmalonate with ethyl tiglate was 15%. Acid hydrolysis of the condensation product gave an oil, but alkaline hydrolysis yielded a solid tribasic acid, $C_{10}H_{16}O_6$, m. p. 159°; on admixture with the acid (IX) a considerable depression of m. p. was observed and, for reasons enumerated below, the substance is considered to be *γ-carboxy-αβ-dimethyl-γ-ethylglutaric acid* (VIII; R = H). Attempted methylation of the condensation product was unsuccessful [(X; R = Et) should be methylated readily], the only substances isolated being 35% of recovered condensation product (identified by hydrolysis to the tribasic acid, m. p. 159°) and 65% of a mixture of retrogression products, which were identified as ethyl tiglate and ethyl methylethylmalonate by conversion into the anilides (IX; R = Et should, and does, give ethyl α-ethylcrotonate as the unsaturated retrogression product on attempted methylation). There is thus no doubt that the condensation product is ethyl γ-carbethoxy-αβ-dimethyl-γ-ethylglutarate (VIII; R = Et), the reaction having proceeded by route (*a*), *i.e.*, normally.

The course of the reaction between ethyl α-ethylcrotonate and ethyl methylmalonate is even clearer. A 40% yield of condensation product was obtained which, on alkaline hydrolysis, gave α-carboxy-αβ-dimethyl-γ-ethylglutaric acid (IX; R = H), m. p. 161° alone or mixed with an authentic specimen. Acid hydrolysis yielded αβ-dimethyl-γ-ethylglutaric acid (XI), m. p. 123°, not depressed on admixture with the synthetic material. Attempted methylation of the condensation product brought about complete retrogression to a mixture of ethyl α-ethylcrotonate and ethyl dimethylmalonate, both of which were identified as the corresponding anilides. It is evident, therefore, that the condensation product is ethyl α-carbethoxy-αβ-dimethyl-γ-ethylglutarate (IX; R = Et), having been formed, normally, by route (*a*).

Thus, all the reactions examined in this paper have been shown to proceed by route (*a*), *i.e.*, by the normal mechanism, and no evidence for any reaction by Thorpe's mechanism [route (*c*)] has been obtained.

Holden and Lapworth's mechanism (J., 1931, 2370) may be generalised in the following scheme (or the analogous scheme in which CN replaces $CO_2Et$ and C:NH replaces CO):



(A.) (B.) (C.)

in which (A) is the normal addition product, which, it is assumed, is always the initial product of the reaction; (B) is a hypothetical intermediate keto-ester derived from one or

more molecules of (A) by a ring closure of the Dieckmann type [the two keto-groups in the formula may be one and the same, in which case (B) is a *cyclo*butanone derivative]; and (C) is an isomer of (A) in which apparent migration of a carbethoxyl group has taken place, and which is formed by alcoholysis of (B) by the alternative to the route (B) $\longrightarrow$ (A).

Holden and Lapworth regarded the successive reactions (A) $\rightleftarrows$ (B) $\rightleftarrows$ (C) as equilibria and pointed out that the series of reactions is likely to proceed from left to right if (a) the labile H in (A) is one of a pair attached to the same carbon atom and (b) the labile H in (C) is solitary. Further consideration of these conditions enables certain predictions to be made as to what types of reaction will show abnormality and what types will be normal. It should be pointed out, with Holden and Lapworth, that abnormality of the type encountered by Howles, Thorpe, and Udall (J., 1900, **77**, 943) in the condensation of ethyl α-methylacrylate with ethyl sodiocyanoacetate is of a different type and explicable in quite another way not involving this series of changes.

Condition (a) ($R' = H$) is the necessary condition for any keto-ester formation, *i.e.*, only if $R' = H$ will the reaction (A) $\longrightarrow$ (B) take place. Thus, if $R' = H$, the reaction *may* be abnormal; if $R' \neq H$, the reaction *must* be normal.

Condition (b) ($R'' \neq H$) is the condition for preferential fission of (B) to give (C) rather than (A). Now we have just shown that (B) is only formed if $R' = H$. With this proviso, if $R'' = H$, the reaction *may* be abnormal, whereas if $R'' \neq H$, the reaction *must* be abnormal.

Holden and Lapworth's theory thus requires normal reaction when $R' \neq H$ (whether or not $R'' = H$), abnormal reaction when $R' = H$ and $R'' \neq H$, and makes no prediction when $R' = R'' = H$.

We are thus led to formulate the following two general rules:

(i) All condensations of unsaturated compounds of the type $CR_2{:}CR'X$ with malonic esters (and similar substances) and their alkyl derivatives will be normal [route (*a*)].

(ii) All condensations of unsaturated compounds of the type $CR_2{:}CHX$ with alkylmalonic esters (and similar compounds) will be abnormal [route (*b*)].

Rule (i) is fulfilled by the three condensations described in this paper, in all of which the unsaturated reactant is an α-substituted unsaturated ester and all of which have been shown to be normal. Neither, so far as we are aware, has any exception to this rule been found in any well-authenticated case.

To rule (ii) conform the additions of alkylmalonic esters to ethyl fumarate, which are known to be abnormal (Michael and Ross, *J. Amer. Chem. Soc.*, 1931, **53**, 1150; Duff and Ingold, J., 1934, 87; Rydon, J., 1935, 420; Ingold and Rydon, *ibid.*, p. 857; Part II, this vol., p. 42); the abnormal additions of ethyl α-cyanopropionate to ethyl ββ-dimethylacrylate (Thorpe, J., 1900, **77**, 923) and to ethyl crotonate (Michael and Ross, *J. Amer. Chem. Soc.*, 1931, **53**, 1150) and the abnormal additions of ethyl methylmalonate to crotonic and cinnamic esters (Michael and Ross, *J. Amer. Chem. Soc.*, 1930, **52**, 4598) and to benzylideneacetophenone (Holden and Lapworth, *loc. cit.*). There are, however, two apparent exceptions among well-authenticated reactions of this type. The first of these is the normality of a number of additions of alkylmalonic esters to acetylenic esters of the type $CR{:}C{\cdot}CO_2Et$, which has been clearly shown by Farmer, Ghosal, and Kon (J., 1936, 1804). These acetylenic esters, however, contain no α-hydrogen, and the mobile hydrogen in (A) is, therefore, not one of a pair; in fact, they may be regarded as α-substituted ethylenic esters, the α-substituent being the β-carbon atom and the group R which it carries. Once this is clear it is evident that rule (i) and not rule (ii) is applicable and the observed normality falls into line with the theory. The other exception to rule (ii) is the normality of the addition of ethyl benzylmalonate to αβ-dibenzoylethylene; this is, no doubt, to be ascribed to the insolubility of the initial product (A) in the reaction medium, which results in its removal from active participation in the reaction before any conversion into the intermediate (B) can take place.

To sum up, in spite of the absence of very clear and definite evidence as to the mechanism of abnormal cases of the Michael reaction, the success of Holden and Lapworth's theory in predicting the occurrence of such abnormal reactions seems to us sufficient evidence, on pragmatic grounds, of its validity. It is, perhaps, hardly necessary to add that

of sodium ethoxide or, more strictly, an amount sufficient to bring about the series of reactions (A) $\rightleftarrows$ (B) $\rightleftarrows$ (C); additions in the presence of small, "catalytic" amounts of ethoxide doubtless proceed by quite a different mechanism to which the theory is not, and was not intended to be, applicable.

## EXPERIMENTAL.

*Synthesis of* cyclo*Hexane-1-carboxylic-2-α-propionic Acid.*—17 G. of ethyl *cyclo*hexane-1-carboxylate-2-malonate (Helfer, *Helv. Chim. Acta*, 1926, **9**, 816; Boorman and Linstead, J. 1935, 261) were added to 1·25 g. of "molecular" sodium under light petroleum (b. p. 60—80°) formation of the sodio-derivative was complete after 2 hours' refluxing. 35 G. of methyl iodide were added, and the mixture refluxed for a further 3 hours. The sodium iodide was filtered off and the filtrate washed with water, dried, and distilled, yielding 12·8 g. (72%) of ethyl *cyclo*hexane-1-carboxylate-2-methylmalonate (III; R = Et), b. p. 164—166°/3 mm., $n_D^{16°}$ 1·4647, $d_{4°}^{16°}$ 1·0828, $[R_L]_D$ 83·70 (calc., 83·47).

*Acid hydrolysis.* 8 G. of the above ester (III; R = Et) were refluxed for several days with 40 c.c. of concentrated hydrochloric acid. The solution was boiled with charcoal and filtered; on cooling, 2·9 g. (60%) of solid acid, m. p. 165—169°, were deposited. Three crystallisations from dilute acetic acid yielded cyclo*hexane*-1-*carboxylic*-2-α-*propionic acid* (VI) in clusters of small prisms, m. p. 184° [Found: C, 60·1; H, 8·2; equiv. (by titration), 100·1. $C_{10}H_{16}O_4$ (dibasic) requires C, 60·0; H, 8·0%; equiv., 100·0]. 0·8 G., heated in a sealed tube with 10 c.c. of concentrated hydrochloric acid for 40 hours, gave, on crystallisation, 0·45 g. of an acid, m. p. 172—175° [mixed m. p. with (VI), 175—178°], and 0·15 g. of an acid, m. p. 130—135° [mixed m. p. with (VI), 135—139°], indicating a partial conversion into a stereoisomeride, presumably *trans-trans* (cf. p. 49).

*Alkaline hydrolysis.* 5 G. of the ester (III; R = Et) were refluxed overnight with 25 c.c. of 30% alcoholic potassium hydroxide. The alcohol was removed, and the residue taken up in water, acidified and extracted with ether. 3·3 G. of an acid which quickly solidified were obtained. This was fractionally crystallised from water, yielding 0·8 g. of the dicarboxylic acid (VI), m. p. 184°, and 1·2 g. of a mixture of acids, m. p. 170—173°, which could not be further separated and was shown by analysis to be a mixture of the dibasic acid (VI) and the desired tribasic acid (III; R = H) (Found: C, 56·9; H, 7·3. Calc. for $C_{10}H_{16}O_4$: C, 60·0; H, 8·0%. Calc. for $C_{11}H_{16}O_6$: C, 54·1; H, 6·5%).

*Attempted methylation.* 5 G. of the ester (III; R = Et) were added to 0·35 g. of "molecular" sodium in benzene. The initial slight reaction quickly abated and 4 hours' refluxing was necessary to complete the solution of the sodium. 10 G. of methyl iodide were added, sodium iodide being precipitated at once. Refluxing was continued overnight, and the product worked up in the usual manner. The following fractions were collected: (1) b. p. 96—104°/20 mm. 1·8 g.; (2) 100—156°/2 mm., 0·5 g.; (3) 156—158°/2 mm., 0·9 g. Fraction (1) was identified as ethyl dimethylmalonate by conversion into the anilide with anilinomagnesium bromide (Hardy J., 1936, 398; cf. Bodroux, *Compt. rend.*, 1904, **138**, 1427). One crystallisation of the product from alcohol gave pure dimethylmalonanilide, m. p. 202°, identified by mixed m. p. with a specimen prepared similarly from authentic ethyl dimethylmalonate. Fraction (3) was refluxed with 10 c.c. of concentrated hydrochloric acid for 40 hours. 0·4 G. of acid crystallised from the cooled solution; two crystallisations from dilute acetic acid raised the m. p. to 178—180°, mixed m. p. with the acid (VI), 179—181°; fraction (3) thus consisted of unchanged ester (III; R = Et).

*Ethyl Δ¹-Tetrahydrobenzoate.*—In the preparation of Δ¹-tetrahydrobenzoic acid from Δ¹-tetrahydrobenzonitrile by the method of Boorman and Linstead (J., 1935, 261) steam-distillation was found to be unnecessary. The solid acid was refluxed with a 10% excess of thionyl chloride for an hour, and the crude chloride poured into absolute alcohol (3 vols.). After refluxing for an hour, the mixture was poured into water and extracted with ether. Distillation of the dried extract gave a 90% yield of pure ethyl Δ¹-tetrahydrobenzoate, b. p. 95—97°/15 mm., $n_D^{15°}$ 1·4716, $d_{4°}^{15°}$ 1·0018, $[R_L]_D$ 43·01 (calc., 42·75) (Boorman and Linstead, *loc. cit.*, give $n_D^{20°}$ 1·4700, $d_{4°}^{20°}$ 0·9999 for a specimen prepared through the silver salt).

Ethyl methylmalonate was prepared from ethyl α-bromopropionate through the cyano-ester by Steele's method (*J. Amer. Chem. Soc.*, 1931, **53**, 286); b. p. 94°/16 mm.; $n_D^{15·8°}$ 1·4148, $d_{4°}^{15·8°}$ 1·0256, $[R_L]_D$ 42·46 (calc., 42·45) (Auwers, *Ber.*, 1913, **46**, 509, gives $n_D^{18·7°}$ 1·4137, $d_{4°}^{18·7°}$ 1·0192).

***Condensation of Ethyl Δ¹-Tetrahydrobenzoate with Ethyl Methylmalonate.***—Sodium (1 equiv.) was dissolved in ten times its weight of absolute alcohol, and equivalent weights of ethyl methyl-

malonate and ethyl $\Delta^1$-tetrahydrobenzoate added to the solution. The mixtures were left in the cold and/or heated on the steam-bath for various times. They were then poured into much water, acidified, and extracted with ether. The extract was washed with 10% sodium carbonate solution and water, dried, and distilled. After a large low fraction, consisting of unchanged reactants, the product was collected at 160—166°/2 mm. The yields under various conditions were: ½ hour on steam-bath, trace; 2 days in the cold, trace; 20 hours on steam-bath, 2 days in the cold, 2%; 6 days in the cold, 17 hours on steam-bath, 3%; 5 days in the cold, 7½ hours on steam-bath, 4%; 8 days in the cold, 5%; 3 days in the cold, 24 hours on steam-bath, 5%; 56 hours on steam-bath, 6%. The various high fractions were combined and redistilled. The condensation *product* had b. p. 158—160°/1·5 mm., $n_D^{20·6°}$ 1·4627, $d_{4°}^{20·6°}$ 1·0789, $[R_L]_D$ 83·69 (calc., 83·47) (Found: C, 62·1; H, 8·7. $C_{17}H_{28}O_6$ requires C, 62·2; H, 8·5%).

*Hydrolysis*. 5 G. of the condensation product were refluxed overnight with 30 c.c. of 30% alcoholic potassium hydroxide. The alcohol was removed and the residue treated with water, acidified, and extracted with ether. Evaporation of the dried extract yielded 2·6 g. of an oil which rapidly solidified. Five crystallisations from water yielded 1·1 g. of pure dibasic acid, m. p. 184° (Found: C, 60·2; H, 8·05. Calc. for $C_{10}H_{16}O_4$: C, 60·0; H, 8·0%). Admixture with either form of 1-methyl*cyclo*hexane-1-carboxylic-2-acetic acid (VII) depressed the m. p. to 140—150°, whereas a mixture with the synthetic *cyclo*hexane-1-carboxylic-2-α-propionic acid (VI) was unchanged in m. p.

*Attempted methylation*. 5 G. of the addition product were added to 0·35 g. of pulverised sodium suspended in dry benzene. The initial slight reaction soon abated and 4 hours' refluxing was required to bring the sodium into solution. 10 G. of methyl iodide were added, and the mixture refluxed overnight. It was then poured into water and extracted with ether. Distillation of the dried extract at 4 mm. gave three fractions: (1) b. p. 80—120°, 1·9 g.; (2) b. p. 120—168°, 0·2 g.; (3) b. p. 168—173°, 1·2 g. Fraction (1) was identified as ethyl dimethylmalonate by conversion into the dianilide, m. p. and mixed m. p. 202°, by Hardy's method. Fraction (3) was identified as unchanged starting material by refluxing with 10 c.c. of concentrated hydrochloric acid: extraction with ether gave 0·48 g. (60%) of crude acid, m. p. 165—170°; two crystallisations raised the m. p. to 179—181°, mixed m. p. with the acid (VI) 180—182°.

*Ethyl Tiglate* (cf. Ray, *J. Amer. Chem. Soc.*, 1928, **50**, 560).—135 G. of methylethylacetic acid (Gilman and Parker, *Org. Synth.*, 1925, **5**, 75) were treated with 120 c.c. of thionyl chloride, and the mixture refluxed for an hour on the steam-bath. 225 G. of bromine were then added dropwise, and heating continued till all the bromine had reacted. The cooled product was poured into 150 c.c. of absolute alcohol and refluxed for an hour. It was then poured into water and extracted with ether. The extract was washed with 10% sodium carbonate solution and water, dried, and distilled; yield of ethyl methylethylbromoacetate, b. p. 73—76°/14 mm., 230 g. (86%). This was refluxed for 2 hours with 127 g. of dimethylaniline and kept overnight. The ester was decanted, taken up in ether, and washed successively with dilute hydrochloric acid, 10% sodium carbonate solution, and water. Careful distillation of the dried extract yielded 110 g. (78%) of pure ethyl tiglate, b. p. 55—57°/15 mm., $n_D^{18·8°}$ 1·4347, $d_{4°}^{18·8°}$ 0·9239, $[R_L]_D$ 36·13 (calc., 35·71) (Auwers and Wissebach, *Annalen*, 1923, **432**, 71, give b. p. 55·5°/11 mm., $n_D^{19·5°}$ 1·4355, $d_{4°}^{19·5°}$ 0·9247).

*Synthesis of αβ-Dimethyl-γ-ethylglutaric Acid*.—24 G. of ethyl tiglate and 30 g. of ethyl malonate were added to sodium ethoxide [from sodium (4·6 g.) and ethyl alcohol (70 c.c.)], and the solution kept for 14 days. It was then poured into water and extracted with ether, and the extract washed with 10% sodium carbonate solution and water. Distillation of the dried extract yielded 34 g. (63%) of ethyl γ-carbethoxy-αβ-dimethylglutarate, b. p. 147—150°/3 mm. (Found: C, 58·7; H, 8·4. Calc. for $C_{14}H_{24}O_6$: C, 58·3; H, 8·3%).

An attempt to ethylate this product with the aid of "molecular" sodium in light petroleum (b. p. 60—80°) was unsuccessful. Accordingly, 1·6 g. of sodium, suspended in ether, were treated with 4·0 c.c. of absolute alcohol, and the mixture kept overnight. When 19·2 g. of the above ester were added, the sodium ethoxide dissolved almost immediately. 13 G. of ethyl iodide were added and, after standing at room temperature overnight, the mixture was refluxed on the steam-bath until neutral (6 hours). Working-up in the usual manner gave 13·5 g. (64%) of *ethyl γ-carbethoxy-αβ-dimethyl-γ-ethylglutarate* (VIII; R = Et), b. p. 145—146°/2 mm., $n_D^{18·8°}$ 1·4430, $d_{4°}^{18·8°}$ 1·0480, $[R_L]_D$ 80·02 (calc., 81·05) (Found: C, 60·6; H, 8·9. $C_{16}H_{28}O_6$ requires C, 60·8; H, 8·8%).

*Ethyl α-Ethylcrotonate* (cf. Auwers and Meissner, *Annalen*, 1923, **432**, 76).—75 G. of diethylacetic acid (Conrad, *Annalen*, 1880, **204**, 141) were treated with 84 g. of thionyl chloride and refluxed for an hour; while steam-heating continued, 35 c.c. of bromine were added dropwise

very slowly. When the colour of the bromine had vanished, the liquid was cautiously poured into 120 c.c. of absolute alcohol and refluxed for an hour. The product was poured into water extracted with ether, washed with 10% sodium carbonate solution and water, dried, and distilled; yield of ethyl α-bromodiethylacetate, b. p. 78—81°/9 mm., 105 g. (85%). This was refluxed for 2 hours with 150 g. of dimethylaniline, and the product poured into dilute hydrochloric acid and extracted with ether. The extract was washed with 10% sodium carbonate solution and water, dried, and distilled, affording 54 g. (80%) of ethyl α-ethylcrotonate, b. p. 62—64°/12 mm., $n_D^{17°}$ 1·4339, $d_{4°}^{17°}$ 0·9071, $[R_L]_D$ 40·76 (calc., 40·33).

*Synthesis of αβ-Dimethyl-γ-ethylglutaric Acid.*—21 G. of ethyl α-ethylcrotonate and 23 g. of ethyl malonate were added to sodium ethoxide (from 3·3 g. of sodium and 40 c.c. of absolute alcohol). After 14 days the product was poured into water, extracted with ether, and washed with 10% sodium carbonate solution and water. Distillation of the dried extract yielded 21 g. (48%) of *ethyl α-carbethoxy-β-methyl-γ-ethylglutarate*, b. p. 148—150°/3 mm. (Found : C, 59·5; H, 8·7. $C_{15}H_{26}O_6$ requires C, 59·6; H, 8·6%).

20 G. of this ester were added to ethereal sodium ethoxide (from 1·6 g. of sodium and 4·0 c.c. of absolute alcohol). The sodium ethoxide dissolved at once and 12 g. of methyl iodide were added. After 12 hours the product was refluxed until neutral (4 hours), poured into water, and worked up. Distillation gave 14 g. (67%) of *ethyl α-carbethoxy-αβ-dimethyl-γ-ethylglutarate* (IX; R = Et), b. p. 154—156°/4 mm., $n_D^{18·8°}$ 1·4430, $d_{4°}^{18·8°}$ 1·0432, $[R_L]_D$ 80·34 (calc., 81·05) (Found : C, 60·5; H, 8·8. $C_{16}H_{28}O_6$ requires C, 60·8; H, 8·8%).

*Alkaline hydrolysis.* 4 G. of the above ester were refluxed for 4 days with 6 g. of potassium hydroxide in 20 c.c. of alcohol. On removal of the alcohol, solution of the residue in water acidification and extraction, 2·0 g. of an oil were obtained which slowly solidified. After being washed with chloroform, the solid had m. p. 140—145°; two crystallisations from chloroform acetone yielded *α-carboxy-αβ-dimethyl-γ-ethylglutaric acid* (IX; R = H) in short prisms, m. p. 161° [Found : C, 51·3; H, 7·0; equiv. (by titration), 77·2. $C_{10}H_{16}O_6$ (tribasic) requires C, 51·7; H, 6·9%; equiv., 77·3].

*Acid hydrolysis.* 5 G. of the ester (IX; R = Et) were refluxed for a week with 50 c.c. of concentrated hydrochloric acid. The residual oil was removed with charcoal, and the filtrate evaporated. 1·3 G. of an oil were obtained which rapidly solidified; two crystallisations from benzene–light petroleum, followed by one from water, yielded *αβ-dimethyl-γ-ethylglutaric acid* (XI) in clusters of prisms, m. p. 123° (Found : C, 57·2; H, 8·9. $C_9H_{16}O_4$ requires C, 57·4; H, 8·5%).

*Ethyl Ethylmalonate.*—The following is based on the method of Michael (*J. pr. Chem.*, 1905, **72**, 548) : Crude ethyl ethylmalonate (235 g.), b. p. 102°/18 mm.—98°/11 mm., prepared by ethylation of ethyl malonate in ethereal solution, was shaken for 30 minutes with 130 c.c. of 25% potassium hydroxide solution. The aqueous layer was run off, and the residue boiled with a solution of 75 g. of potassium hydroxide in 300 c.c. of water for an hour. After cooling and separation, the ester was run carefully, with mechanical stirring, into 90 c.c. of water containing 75 g. of potassium hydroxide, and the mixture kept overnight. Unchanged diethylmalonic ester was removed by three extractions with ether. The water layer was then added to 140 g. of potassium hydroxide in 500 c.c. of water, and the whole was boiled for 2 hours, diluted to 3 l., neutralised with hydrochloric acid, and made just alkaline with ammonia, and 500 c.c. of saturated calcium chloride solution added to the hot solution. After several hours' heating on the steam-bath the calcium salt was filtered off, dried, suspended in 500 c.c. of absolute alcohol and dry hydrogen chloride passed in to saturation. The solution was refluxed for 6 hours poured into water, and extracted with ether. The extract was washed with 10% sodium carbonate solution and water and dried. Distillation gave 100 g. of pure ethyl ethylmalonate b. p. 98—99°/12 mm., $n_D^{14°}$ 1·4181, $d_{4°}^{14°}$ 1·0101, $[R_L]_D$ 46·91 (calc., 47·07).

*Condensation of Ethyl Tiglate with Ethyl Ethylmalonate.*—43 G. of ethyl tiglate and 63 g. of ethyl ethylmalonate were added to sodium ethoxide [from sodium (7·7 g.) and absolute alcohol (100 c.c.)]. The mixture was left at room temperature for 14 days and then poured into a large volume of water and extracted with ether. Distillation of the dried extract, after washing with 10% sodium carbonate and water, yielded 15 g. (14%) of condensation product, which is considered to be ethyl γ-carbethoxy-αβ-dimethyl-γ-ethylglutarate (VIII; R = Et), b. p. 151—152°/2·5 mm., $n_D^{18·8°}$ 1·4435, $d_{4°}^{18·8°}$ 1·0396, $[R_L]_D$ 80·66 (calc., 81·05) (Found : C, 60·2; H, 8·7. Calc. : C, 60·8; H, 8·8%).

Acidification of the alkaline washings gave an oil from which ethylmalonic and tiglic acids were isolated and identified by mixed m. p.

*Alkaline hydrolysis.* 3 G. of the condensation product were refluxed for 4 days with 5 g.

otassium hydroxide in 20 c.c. of alcohol. The alcohol was removed, and the residue taken up water, acidified, and extracted with ether. Evaporation of the dried extract gave 1·5 g. (0%) of an oil which slowly solidified in a vacuum desiccator. The solid was washed with loroform, and two crystallisations from benzene–acetone–light petroleum then yielded small ibes (0·6 g.), m. p. 158—159°, of a tribasic acid (Found: C, 52·0; H, 7·0. $C_{10}H_{16}O_6$ requires , 51·7; H, 6·9%) which is considered to be *γ-carboxy-αβ-dimethyl-γ-ethylglutaric acid* (VIII; = H).

*Attempted methylation.* 0·6 G. of "molecular" sodium was suspended in dry ether, and 1·5 c. of absolute alcohol added, followed after 12 hours by 8 g. of the above condensation product ith ice-cooling; the sodium ethoxide took nearly 2 hours to dissolve and heating on the steam-ath was necessary to complete solution. 10 G. of methyl iodide were added, sodium iodide eing precipitated immediately; the mixture was kept overnight and poured into water, and the hereal solution separated, washed with 10% sodium carbonate solution and water, dried, and istilled. Four fractions were collected: (1) b. p. 63—75°/18 mm., 1·3 g.; (2) b. p. 100—115°/18 m., 2·4 g.; (3) b. p. 115°/18 mm.—135°/1 mm., 0·2 g.; (4) b. p. 135—140°/1 mm., 2·5 g. raction (1) was identified as ethyl tiglate by conversion by Hardy's method into the anilide, . p. and mixed m. p. 75°. Fraction (2) was similarly identified as ethyl methylethylmalonate y conversion into *methylethylmalondianilide*, m. p. 174° (Found: C, 73·3; H, 6·9. $C_{18}H_{20}O_2N_2$ quires C, 73·0; H, 6·7%), not depressed by a sample similarly prepared from authentic ethyl ethylethylmalonate. Fraction (4) was refluxed for 5 days with 4 g. of potassium hydroxide 15 c.c. of alcohol. After the usual treatment 1·3 g. of a solid acid were obtained, m. p. 140—14°; one recrystallisation from benzene–acetone–light petroleum yielded the same tribasic id (VIII; R = H) as was obtained by hydrolysis of the original condensation product, m. p. d mixed m. p. 159°.

*Condensation of Ethyl Methylmalonate with Ethyl α-Ethylcrotonate.*—40 G. of ethyl α-ethyl-otonate and 49 g. of ethyl methylmalonate were added to a cold solution of sodium ethoxide rom sodium (6·6 g.) and absolute alcohol (70 c.c.)]. The mixture was kept at room temperature r 14 days and then poured into a large volume of water and extracted with ether. Distillation the dried extract, after washing with 10% sodium carbonate solution and water, yielded 35 g. 9%) of condensation product, considered to be ethyl α-carbethoxy-αβ-dimethyl-γ-ethyl-utarate (IX; R = Et), b. p. 152—158°/4 mm. On redistillation it had b. p. 153—155°/3·5 m., $n_D^{18·8°}$ 1·4437, $d_{4°}^{18·8°}$ 1·0399, $[R_L]_D$ 80·67 (calc., 81·05) (Found: C, 60·3; H, 8·9. Calc.: C, )·8; H, 8·8%).

*Acid hydrolysis.* 5 G. of the above addition product were refluxed for a week with 50 c.c. of ncentrated hydrochloric acid. The solution was then boiled with charcoal, filtered, and aporated, yielding 1·8 g. of an oil which partly solidified. The solid was crystallised twice om benzene–light petroleum and once from water, 0·7 g. of αβ-dimethyl-γ-ethylglutaric acid (I) being obtained in long prisms, m. p. and mixed m. p. with an authentic specimen, 123°.

*Alkaline hydrolysis.* 3·6 G. of the above addition product were refluxed for 5 days with g. of potassium hydroxide in 20 c.c. of alcohol. The alcohol was removed, and the residue ken up in water, acidified, and extracted with ether; evaporation of the dried extract yielded 3 g. (80%) of an oil which solidified almost immediately in a vacuum desiccator. After being ashed with cold chloroform, the product had m. p. 145—148°; two crystallisations from loroform–acetone yielded 1·4 g. of α-carboxy-αβ-dimethyl-γ-ethylglutaric acid (IX; R = H), . p. and mixed m. p. with an authentic specimen, 161°.

*Attempted methylation.* 8 G. of the addition product were added to sodium ethoxide (from 6 g. of sodium and 1·5 c.c. of absolute alcohol) in ether. The mixture was refluxed until the dium ethoxide dissolved; the solution was then cooled, and 10 g. of methyl iodide added. here was a vigorous reaction accompanied by the precipitation of sodium iodide; the solution as refluxed overnight and worked up in the usual manner. Distillation at 24 mm. gave two actions: (1) b. p. 70—85°, 2·3 g., and (2) b. p. 85—110°, 3·0 g. There was no appreciable sidue. Fraction (1) was identified as a mixture of ethyl α-ethylcrotonate and ethyl dimethyl-alonate by conversion into the corresponding anilides, m. p. and mixed m. p. 95° and 202°, spectively. Fraction (2) was similarly shown to be ethyl dimethylmalonate by conversion to the anilide, m. p. and mixed m. p. 202°.

We thank the Royal Society and the Chemical Society for grants.

Imperial College, London, S.W.7.
[*Received, November 20th*, 1937.]

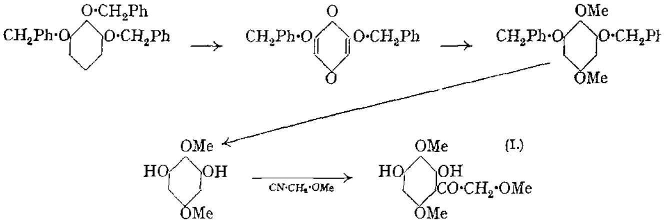
# 14. *Anthoxanthins. Part XVI. Synthesis of Herbacetin.*

By L. J. GOLDSWORTHY and ROBERT ROBINSON.

The new glucoside, herbacitrin, isolated by Seshadri and his collaborators from flowers of certain cotton plants is isomeric with quercimeritrin but has a closer resemblance to gossypitrin in its chemical behaviour. The related aglucone, herbacetin, isomeric with quercetin, is similar to gossypetin, especially in its facile aerial oxidation in alkaline solution. Because herbacitrin could be degraded to anisic acid, and taking into account the analogies already mentioned, the suggestion was made that herbacetin bears to gossypetin the relation that kaempferol bears to quercetin.

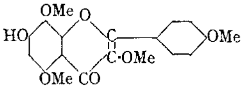
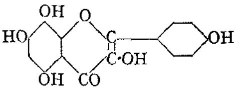
This view that herbacetin is 3 : 5 : 7 : 8 : 4′-pentahydroxyflavone has now been confirmed by unambiguous synthesis following the lines of the method used for the synthesis of gossypetin.

2 : 4-DIHYDROXY-ω : 3 : 6-TRIMETHOXYACETOPHENONE (I) was obtained (Baker, Nodzu, and Robinson, J., 1929, 79) by a method, indicated in the annexed scheme, which gave no scope for doubt as to the constitution of the product.




The point is an important one, because the synthetical proof of the constitution o quercetagetin (there is no complete analytical proof) rests on the exclusion of th alternative structure first assigned to gossypetin. The intermediate ketone (I) is als constructed fortunately in that the aroylation and ring-closure to a flavonol derivativ can proceed in one direction only.

Treatment with veratric anhydride and sodium veratrate afforded a hydroxypenta methoxyflavone which was a pentamethyl ether of gossypetin. Using, in a simila reaction, anisic anhydride and sodium anisate, and working in the usual manner b hydrolysis of the aroylated product, we have now obtained 7-*hydroxy*-3 : 5 : 8 : 4 *tetramethoxyflavone* (II).

(II.)   (III.)


On demethylation by means of boiling hydriodic acid, 3 : 5 : 7 : 8 : 4′-*pentahydroxyflavon* (III) was obtained, and this flavone proved to be identical with herbacetin as describe by Neelakantam and Seshadri (*Proc. Indian Acad. Sci.*, 1937, **5**, Sec. A, No. **4**, 357). W are grateful to Dr. T. R. Seshadri for the provision of specimens of herbacetin and i penta-acetyl derivative which have enabled us to establish the identity by dire comparison.

## EXPERIMENTAL.

7-*Hydroxy*-3 : 5 : 8 : 4′-*tetramethoxyflavone* (II).—An intimate mixture of 2 : 4-dihydrox ω : 3 : 6-trimethoxyacetophenone (I) (1·0 g.), anisic anhydride (4·0 g.), and sodium anisa

(2·0 g.) was heated for 3 hours at 180—185° (oil-bath) under 20 mm. pressure. The cooled product was hydrolysed by refluxing it for 30 minutes with a solution of potassium hydroxide (4·0 g.) in alcohol (30 c.c.) and water (2 c.c.). The bulk of the alcohol was removed on the steam-bath, and the residue shaken with water (50 c.c.). The portion of the residue (0·76 g.) insoluble in water was unhydrolysed material: it was powdered and refluxed with a further quantity (2·0 g.) of potassium hydroxide, dissolved in alcohol (15 c.c.) and water (1 c.c.). After the removal of the alcohol, the residue dissolved completely in water. When carbon dioxide was passed into the combined aqueous solutions, diluted to 100 c.c., the *flavone* was eventually precipitated. No precipitate was formed until a rapid stream of the gas had been passed through the solution for ½ hour. The product was collected, washed well with water, and dried at 100°; m. p. *ca.* 254° with previous sintering. The substance crystallised readily from alcohol in glistening, golden-yellow, thin, rectangular plates, m. p. 268—269° with slight sintering. A second crystallisation from alcohol raised the m. p. to 269—270° (Found in material dried at 100° and finally in a vacuum over sulphuric acid at room temperature: C, 63·9; H, 4·9. $C_{19}H_{18}O_7$ requires C, 63·7; H, 5·1%). The flavone dissolved in concentrated hydrochloric acid and in aqueous alkalis to yellow solutions. It gave no characteristic coloration when treated in alcoholic solution with ferric chloride.

3 : 5 : 7 : 8 : 4′-*Pentahydroxyflavone* (*Herbacetin*, III).—7-Hydroxy-3 : 5 : 8 : 4′-tetramethoxyflavone (0·6 g.) was demethylated by heating for 3 hours at 135—140° with pure hydriodic acid (9 c.c., *d* 1·7). The red crystalline hydriodide, which separated on cooling, was collected on sintered glass and washed with dilute sulphurous acid. The crystals were then decomposed by heating for 15 minutes on the steam-bath. The yellow product separated from aqueous alcohol in microscopic crystals, m. p. 278—280° (Found in air-dried material: loss at 130° in a vacuum, 5·6. Calc. for $C_{15}H_{10}O_7,H_2O$: $H_2O$, 5·6%). Neelakantam and Seshadri (*loc. cit.*) cited elementary analyses of the natural product, crystallised from aqueous alcohol and dried in the air, showing that herbacetin forms a monohydrate.

Although the separation from aqueous alcohol is usually in the form of extremely minute crystals, slow deposition from a more dilute solution affords flat needles as described for herbacetin. These needles can also be obtained by long digestion of the microcrystalline powder with 50% acetic acid (Found in material dried in a vacuum over sulphuric acid: C, 58·4; H, 3·5. Found for material dried at 110° in high vacuum: C, 59·4; H, 3·4. Calc. for $C_{15}H_{10}O_7$: C, 59·6; H, 3·3%). It is very difficult to remove the last traces of water and the dried product is hygroscopic.

Pure herbacetin is stated to have m. p. 280—283° (*loc. cit.*), but the specimen supplied to us, after recrystallisation, had m. p. 279—281° under our conditions, and the best synthetic specimen and a mixture of the natural and the synthetic specimen showed the same behaviour on heating. The sintering, range of temperature during fusion, and the extent of decomposition were identical.

The synthetic flavonol, like the naturally occurring herbacetin, gives a deep red precipitate with lead acetate in aqueous alcohol, and the ferric reaction is dull green. The yellow solution sulphuric acid is devoid of fluorescence.

The colour reactions shown in buffered solutions prepared from "B.D.H. Buffer Salt" ontaining phosphoric, boric, and phenylacetic acids) were found to resemble generally those escribed by Neelakantam and Seshadri (*loc. cit.*, p. 362), but there were slight divergences the observed rates of colour changes. As the processes involved depend on aerial oxidation, ey are affected by the quantity taken, the size of the crystals, the shape of the tubes nployed, the frequency of shaking, and especially by the temperature.

Small specimens of the synthetic and the naturally occurring flavonol were crystallised ıder similar conditions so as to obtain a fine microcrystalline powder. This was shaken ith a buffered solution of $p_H$ 8·0, and approximately equal volumes (*ca.* 1 c.c.) of the ıspensions were added to 20 c.c. of the various buffered solutions in boiling tubes (1 in. iameter) at 14° with only one shaking to mix. Under these conditions the two specimens ıve identical results when compared side by side.

$p_H$ 6·8: The solntions remained colourless during 24 hours.

$p_H$ 8·0: The solid dissolved very slowly to a light yellow solution and after ¾ hour a faint green shade had developed. Later this changed to a weak dull purple.

$p_H$ 8·6: A light yellow solution was quickly formed; this became green in a few minutes and then very slowly went through slaty grey to a violet-blue.

$p_H$ 9·2: The same colour changes as the last-mentioned occurred more rapidly. This

solution becomes purplish in tone more rapidly than those in the ranges on either side because the yellow background is not so much in evidence as in the solution of $p_H$ 9·8.

$p_H$ 9·8 : The change from yellow to green was much quicker and the solution then became gradually bluer and eventually pure blue. After about 1 hour the colour deteriorated to a slaty blue and thereafter progressively diminished in intensity and after 24 hours all coloration had disappeared. It was found in other experiments that the use of relatively more of the flavonol resulted in retention of a dull purple colour even on long keeping.

At $p_H$ 10·4 and $p_H$ 11·0 the same changes occurred but were greatly accelerated. The deep blue solutions obtained at $p_H$ 9·8—11·0 became red on acidification and doubtless contained "herbacetone" analogous to "gossypetone" (A. G. Perkin, J., 1913, **103**, 650).

Identical dyeings on mordanted cotton were obtained from the "natural" and the synthetic specimens. These are doubtless wholly or partly due to herbacetone, because similar colorations were observed on dyeing from an oxidised bath (an alkaline solution kept until it became blue and then neutralised with acetic acid). The dyeings were: weak iron, grey; strong iron, brownish-black; iron and aluminium, dark dull brown; strong aluminium, brown; weak aluminium, fawn.

3 : 5 : 7 : 8 : 4'-*Penta-acetoxyflavone*.—The synthetic pentahydroxyflavone (0·1 g.) was refluxed with acetic anhydride (0·5 c.c.) and a drop of pyridine for 3 hours. After cooling and keeping for a few hours, the derivative crystallised; it was collected and washed with cold alcohol; m. p. 187—190° with slight sintering. On recrystallisation from alcohol, colourless needles, m. p. 189—191°, were obtained (Neelakantam and Seshadri, *loc. cit.*, give m. p. 192—193° for penta-acetylherbacetin) and two further crystallisations did not raise the m. p which was not depressed on admixture of the specimen with anthentic O-penta-acetylherbacet (Found in synthetic derivative: C, 58·5; H, 4·0. Calc. for $C_{25}H_{20}O_{12}$: C, 58·6; H, 3·9%).

3 : 5 : 7 : 8 : 4'-*Pentamethoxyflavone*.—The above tetramethyl ether dissolved readily in war 10% aqueous sodium hydroxide, but a sparingly soluble sodium salt soon separated in yello needles and did not redissolve on heating. On shaking with methyl sulphate the substan was slowly methylated and it was found best to add some acetone; the methyl ether was th quickly formed. It crystallised from aqueous methyl alcohol in slender woolly needles from ethyl acetate in colourless, stouter, prismatic needles, m. p. 156—158° (Found: C, 64· H, 5·4. $C_{20}H_{20}O_7$ requires C, 64·5; H, 5·4%). The *substance* is a good oxonium base and soluble in cold concentrated hydrochloric acid (or in N-hydrochloric acid on heating) to bright yellow solution. The formation of a sparingly soluble, crystalline ferrichlorid platinichloride and picrate was observed.

The woolly needles absorb iodine from aqueous solutions and are coloured dark greenis blue.

Dyson Perrins Laboratory, Oxford University. [*Received, November 24th*, 1937.]

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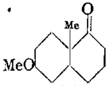
## 15. *The Synthesis of Polyterpenoid Compounds. Part IV.*

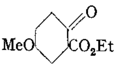
By J. W. Cook and C. A. Lawrence.

It has been shown already that the authors' modification of the Darzens reaction, whereby ring closure is effected in a *cyclo*hexene derivative containing a carboxylated side chain, can be used for the synthesis of 1-ketodecahydronaphthalene derivatives containing an "angular" methyl group. This has been extended in the hope of synthesising 1-keto-6-methoxy-9-methyldecahydronaphthalene, from which a sterol-like molecule might be elaborated. This line of attack was eventually abandoned, as several intermediate stages gave poor yields and ring closure was accompanied by loss of methyl alcohol. Another synthetic route to decahydronaphthalene derivatives has been explored, and several examples are given of the "diene-synthesis" with 1-vinyl-$\Delta^1$-*cyclo*hexene and its 2-methyl derivative, methods of preparation of which are described.

A compound which might prove of service in the synthesis of members of the sterol grou is 6-methoxy-9-methyl-1-decalone (I), and attempts have been made to synthesise thi

etone by extension of the reactions described in Part III (Cook and Lawrence, J., 1937, 17). 4-Methoxy*cyclo*hexanone, obtainable from quinol monomethyl ether (Helfer, *Helv. him. Acta*, **1924**, **7**, 953), was condensed with ethyl oxalate to give *ethyl 4-methoxy*cyclo*xanone-2-glyoxylate*, which underwent thermal degradation to *ethyl 4-methoxy*cyclo*xanone-2-carboxylate* (II). The ensuing condensation with $\gamma$-iodobutyronitrile gave 1 80% yield of *ethyl 4-methoxy-2-$\gamma$-cyanopropyl*cyclo*hexanone-2-carboxylate*, but this on ydrolysis gave only a 25% yield of *$\gamma$-(2-keto-5-methoxy*cyclo*hexyl)butyric acid* (III), so that


(I.)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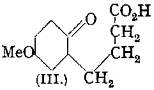
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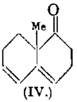
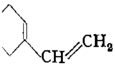
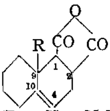
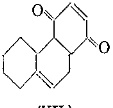

(IV.)

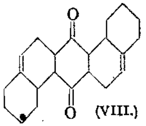
e yield was about 5% with respect to the 4-methoxy*cyclo*hexanone. Methylmagnesium dide interacted with the carbonyl group of the ethyl ester of the keto-acid (III) and the oduct was hydrolysed, dehydrated, and the unsaturated acid cyclised in the customary ay. The reaction was accompanied by elimination of methyl alcohol and the only tonic derivatives isolated from the products were shown by analysis to be derived from ketomethylhexahydronaphthalene, for which formula (IV) may be suggested by analogy ith the known tendency for double bonds to become conjugated and distributed between vo condensed six-membered rings. No material improvement could be effected in the elds of the intermediate products in this synthesis, so further development was considered ipracticable at present, although a different type of method for the synthesis of the keto-id (III) is under investigation.

We thereupon turned our attention to an application of the "diene-synthesis" involvg compounds of the type of 1-*vinyl-$\Delta^1$-*cyclo*hexene* (V), a hydrocarbon which was obtained ithout difficulty by dehydration of 1-*vinyl*cyclo*hexanol* formed by partial hydrogenation 1-ethinyl*cyclo*hexanol, despite the subsequent report of Bergmann and Bergmann (*J. mer. Chem. Soc.*, 1937, **59**, 1446) that they were unable to interrupt the hydrogenation the desired stage. The diene (V) condensed normally with maleic anhydride, and the *lduct* (VI; R = H) was hydrolysed by water to the corresponding carboxylic acid, which as isomerised by alkali and gave a saturated *lactonic acid*.* 1-Vinyl-$\Delta^1$-*cyclo*hexene also acted with *p*-benzoquinone, giving, according to the conditions, 1 : 4-*diketodecahydroienanthrene* (VII) or 9 : 10-*diketo-octadecahydro*-1 : 2 : 5 : 6-*dibenzanthracene* (VIII). The ng system present in the latter compound was established by its dehydrogenation to : 2 : 5 : 6-dibenzanthracene. 1-Vinyl-$\Delta^1$-*cyclo*hexene does not appear to have been tained previously with certainty, although the product obtained by Egorova (*J. Russ. hys. Chem. Soc.*, 1911, **43**, 1122) by isomerisation of vinylidene*cyclo*hexane probably nsists of this hydrocarbon. 1-Vinyl-$\Delta^3$-*cyclo*hexene, which is the principal thermal meride of butadiene, was found by Slobodin (*J. Gen. Chem. Russ.*, 1936, **6**, 129) be isomerised by heated floridin to a mixture of conjugated dienes which reacted with aleic anhydride; this mixture contained chiefly 1-ethylidene-$\Delta^2$-*cyclo*hexene and was parently free from 1-vinyl-$\Delta^1$-*cyclo*hexene.


(V.)


[R = H or Me]
(VI.)


(VII.)


(VIII.)

* At this stage of our work it was stated at a Meeting of the Society that a similar condensation d been carried out with 1-methyl-2-vinyl-$\Delta^1$-*cyclo*hexene by Meggy and Robinson, who used a ferent type of method for the preparation of the diene (*Chem. and Ind.*, 1937, **56**, 512; see also eggy and Robinson, *Nature*, 1937, **140**, 282).

Although Meggy and Robinson (*loc. cit.*) had anticipated us in the logical extension of our work to 1-methyl-2-vinyl-$\Delta^1$-*cyclo*hexene, nevertheless for comparative purposes we prepared this diene by our own method and condensed it with maleic anhydride. The resulting adduct (VI; R = Me) and the corresponding dicarboxylic acid had m. p.'s which tallied approximately with those cited by Meggy and Robinson, and in this case alkali did not produce isomerisation.

In the meantime the synthesis of an œstrogenic hormone by the types of reaction with which we have been concerned has been brought several stages nearer fulfilment by the appearance of two interesting papers (Dane *et al.*, *Annalen*, **1937**, **532**, 29, 39) in which it is shown that 6-methoxy-1-ethinyl-3 : 4-dihydronaphthalene and 1-methyl-$\Delta^1$-*cyclo*pentene-4 : 5-dione can function as components in the Diels–Alder reaction, although the crucial experiment of combining them with each other does not yet appear to have been attempted. In view of the publication of these papers we are not continuing our experiments in this direction.

## Experimental.

*Ethyl 4-Methoxy*cyclo*hexanone-2-glyoxylate*.—4-Methoxy*cyclo*hexanone was prepared by oxidation of 4-methoxy*cyclo*hexanol (Helfer, *Helv. Chim. Acta*, 1924, **7**, 953). We are indebted to Messrs. Howards and Sons, Ltd., for their kindness in hydrogenating quinol monomethyl ether to 4-methoxy*cyclo*hexanol.

A mixture of 4-methoxy*cyclo*hexanone (12·8 g.) and ethyl oxalate (16 g.) was cooled in a freezing mixture and treated gradually with a well-cooled solntion of sodinm (2·5 g.) in alcohol (50 c.c.). After being kept at 0° for 48 hours, the reaction mixture was decomposed with ice-cold dilute sulphuric acid, and the product extracted with ether. The crude ester remaining after removal of the solvent from the washed and dried extract was used for thermal degradation. An analytical sample of the glyoxylic ester was purified through its cupric derivative, which separated when a mixture of the ester and saturated aqueous cupric acetate wa kept overnight. The *cupric* compound crystallised from alcohol in light green, microscopic diamond-shaped plates, m. p. 161—163° (decomp.) [Found: C, 51·05; H, 5·9; Cu, 12·2 $(C_{11}H_{15}O_5)_2Cu$ requires C, 51·0; H, 5·8; Cu 12·3%]. *Ethyl 4-methoxy*cyclo*hexanone-2-glyoxylate* was isolated from the cupric compound by shaking with ether and ice-cold dilut sulphuric acid, and formed a colourless viscous liquid, b. p. 116°/0·4 mm., which gave a cherry red colour with alcoholic ferric chloride (Found: C, 57·3; H, 7·2. $C_{11}H_{16}O_5$ requires C, 57·9 H, 7·1%). The *bis*-2 : *4-dinitrophenylhydrazone* formed thin, orange-yellow, microscopic needle (from aqueous dioxan), m. p. 224—227° (decomp.) (Found: C, 46·9; H, 4·3; N, 18·9 $C_{23}H_{24}O_{11}N_8$ requires C, 46·9; H, 4·2; N, 19·0%).

*Ethyl 4-Methoxy*cyclo*hexanone-2-carboxylate* (II).—The crude glyoxylic ester was boile under reflux until a test portion gave a purple colour with alcoholic ferric chloride (abou 20 minutes), and the product was distilled in a vacuum. The yield of pure *ethyl 4-methox*cyclo*hexanone-2-carboxylate* (II), b. p. 131—133°/10 mm., was about 25% (Found: C, 60· H, 8·3. $C_{10}H_{16}O_4$ requires C, 60·0; H, 8·05%). Its 2 : *4-dinitrophenylhydrazone* formed th golden-yellow plates (from alcohol), m. p. 129—131° (decomp.) (Found: C, 50·6; H, 5· N, 14·9. $C_{16}H_{20}O_7N_4$ requires C, 50·5; H, 5·3; N, 14·7%).

*Ethyl 4-methoxy-2-γ-cyanopropyl*cyclo*hexanone-2-carboxylate* was obtained in 80% yie when a mixture of γ-iodobutyronitrile (8·2 g.) and the sodio-compound prepared from the ket ester (II) (8·4 g.) and powdered sodium (0·95 g.) in benzene (40 c.c.) was heated on the wat bath for 24 hours. It formed a colourless viscous liquid, b. p. 155°/0·2 mm. (Found: C, 62· H, 8·1. $C_{14}H_{21}O_4N$ requires C, 62·9; H, 7·9%), and gave a 2 : *4-dinitrophenylhydrazone* whi crystallised from methyl alcohol in yellow parallelogram-shaped plates, m. p. 123—126° (Foun C, 53·7; H, 5·6; N, 15·9. $C_{20}H_{25}O_7N_5$ requires C, 53·7; H, 5·6; N, 15·65%).

*γ-(2-Keto-5-methoxy*cyclo*hexyl)butyric Acid* (III).—Ethyl 4-methoxy-2-γ-cyanopropylcyc hexanone-2-carboxylate (11·8 g.) was heated on the water-bath for 3 hours with aque potassium hydroxide (9 g. in 250 c.c.). Neutral material was extracted with ether, and t alkaline solution was acidified, saturated with sodium chloride, and extracted with ether twe times. The dried extract was distilled and two fractions collected: (i) b. p. 175—185°/0·6 m (2·2 g.); (ii) b. p. 260—275°/0·6 mm. (4·75 g.). Fraction (i) was the desired *γ-(2-keto-5-metho*cyclo*hexyl)butyric acid* (III), which was purified through the semicarbazone and then forme colourless viscous liquid, b. p. approx. 185°/1 mm., which had not crystallised after seve months (Found: C, 62·3; H, 8·7. $C_{11}H_{18}O_4$ requires C, 61·7; H, 8·5%). Its *semicarbaz*

·rmed microscopic needles (from alcohol), m. p. 178—178·5° after slight sintering (Found : 53·3; H, 7·8. $C_{12}H_{21}O_4N_3$ requires C, 53·1; H, 7·8%). Fraction (ii), the major product, ›peared to be an *anhydride* of a γ-2-keto*cyclo*hexenylbutyric acid resulting from elimination methyl alcohol. After redistillation it formed a very viscous, brownish liquid, b. p. 251—30°/0·4 mm. (Found : C, 69·2, 69·2; H, 7·9, 8·0. $C_{20}H_{26}O_5$ requires C, 68·9; H, 7·5%). On ·drolysis with alkali this anhydride yielded an acid, which was distilled at 0·6 mm. from a ·th at 200° and then gave a *semicarbazone* which crystallised from alcohol in short colourless ·edles, m. p. 219—220·5° (Found : C, 55·3; H, 7·4. $C_{11}H_{17}O_3N_3$ requires C, 55·2; H, 7·15%). ·hen the anhydride was heated with a little baryta at 280—290° in a vacuum, it gave a distillate hich formed a *semicarbazone*, apparently of an isomeric γ-2-keto*cyclo*hexenylbutyric acid, hich crystallised from alcohol in rosettes of microscopic plates, m. p. 213·5—215° (decomp.), ·pressed by the isomeric semicarbazone (Found : C, 55·4; H, 7·4; N, 17·6. $C_{11}H_{17}O_3N_3$ quires C, 55·2; H, 7·15; N, 17·5%). The yield of the desired keto-acid (III) was not improved hen the hydrolysis of the cyano-ester was carried out with concentrated hydrochloric acid.

1-*Keto-9-methylhexahydronaphthalene* (IV ?).—γ-(2-Keto-5-methoxy*cyclo*hexyl)butyric acid ·7 g.) was esterified with alcohol (30 c.c.) and concentrated sulphuric acid (0·7 c.c.), giving ı ethyl ester which formed an almost colourless oil, b. p. 145°/0·2 mm. This ester (4·7 g.) as condensed with methylmagnesium iodide exactly as described in Part III (J., 1937, 821) r the ester of γ-2-keto*cyclo*hexylbutyric acid, and the resulting γ-(5-methoxy-2-methyl-Δ¹-*clo*hexenyl)butyric acid (1·6 g.; b. p. 160—165°/0·8 mm.) was submitted to the general ·ocedure for cyclisation described in Part II (J., 1935, 1637). The neutral product (0·65 g.; p. 150°/30 mm.) gave small yields of a 2 : 4-*dinitrophenylhydrazone*, which crystallised from ıueous dioxan in microscopic, vermilion, diamond-shaped plates, m. p. 224° (decomp.) (Found : , 59·7; H, 4·8. $C_{17}H_{18}O_4N_4$ requires C, 59·6; H, 5·3%), and a *semicarbazone*, which formed microcrystalline powder (from dilute dioxan), m. p. 214—216° (decomp.) in a preheated bath ·ound : C, 65·4; H, 7·5. $C_{12}H_{17}ON_3$ requires C, 65·7; H, 7·8%). The analytical figures dicate that these are derivatives of 1-keto-9-methylhexahydronaphthalene.

### "*Diene*" *Condensations.*

1-*Vinyl*cyclo*hexanol*.—1-Ethinyl*cyclo*hexanol was prepared from *cyclo*hexanone and acetylene described by Pinkney, Nesty, Wiley, and Marvel (*J. Amer. Chem. Soc.*, 1936, **58**, 974) and had p. 85—87°/28 mm. Its p-*nitrobenzoate* formed small lath-shaped crystals (from aqueous ethyl alcohol), m. p. 64—64·5° (Found : C, 65·95; H, 5·6. $C_{15}H_{15}O_4N$ requires C, 65·9; , 5·5%), and its 3 : 5-*dinitrobenzoate* formed thin irregular plates (from ethyl alcohol), m. p. )4·5—106° (Found : C, 56·5; H, 4·5. $C_{15}H_{14}O_6N_2$ requires C, 56·6; H, 4·4%).

A solution of 1-ethinyl*cyclo*hexanol (31·1 g.) in ethyl alcohol (250 c.c.) was shaken with ·drogen in presence of palladium-black (0·3 g.) until 5·5 l. had been absorbed at 24·5° and 772 m. The resulting colourless liquid (26 g.; b. p. 76—79°/25 mm.) gave a p-*nitrobenzoate* ·ystallising in long colourless needles (from aqueous methyl alcohol), m. p. 101—102° (Found : , 65·7; H, 6·4. $C_{15}H_{17}O_4N$ requires C, 65·4; H, 6·2%), and a 3 : 5-*dinitrobenzoate*, which ·rmed thin irregular plates, m. p. 122—123° (from alcohol) (Found : C, 56·4; H, 5·1. $_{15}H_{16}O_6N_2$ requires C, 56·2; H, 5·0%). 1-*Vinyl*cyclo*hexanol*, obtained by hydrolysis of the nitrobenzoate, formed a colourless liquid, b. p. 67—68°/10 mm., which absorbed approximately ·e calculated amount of bromine (Found : C, 75·4; H, 11·5. $C_8H_{14}O$ requires C, 76·1; H, ·2%).

For comparative purposes the esters of 1-ethyl*cyclo*hexanol (Wallach, *Annalen*, 1908, **360**, ); Sabatier and Maihle, *Ann. Chim.*, 1907, **10**, 544) were prepared. Its p-*nitrobenzoate* formed ng slender needles (from aqueous methyl alcohol), m. p. 73—74° (Found : C, 65·1; H, 7·0. $_{15}H_{19}O_4N$ requires C, 64·95; H, 6·9%), and its 3 : 5-*dinitrobenzoate* formed thin irregular ates (from alcohol), m. p. 127—127·5° (Found : C, 55·9; H, 5·8. $C_{15}H_{18}O_6N_2$ requires C, ·9; H, 5·6%). Clearly these esters suffice to characterise the three carbinols and to establish ·e individuality of the vinyl compound, although mixed m. p.'s of corresponding esters showed · depressions.

1-*Vinyl*-Δ¹-cyclo*hexene* (V).—1-Vinyl*cyclo*hexanol (4·2 g.), purified through its *p*-nitro-·nzoate, was heated with potassium hydrogen sulphate (5 g.) at 180° for an hour in an mosphere of nitrogen. The resulting 1-*vinyl*-Δ¹-cyclo*hexene* formed a colourless mobile ·uid, b. p. 145°, with an odour resembling that of butadiene (Found : C, 88·1; H, 11·2. $_8H_{12}$ requires C, 88·8; H, 11·2%).

Δ$^{4:10}$-*Octahydronaphthalene*-1 : 2-*dicarboxylic Anhydride* (VI; R = H).—A mixture of vinyl-Δ¹-*cyclo*hexene (0·5 g.), maleic anhydride (0·35 g.), and xylene (3 c.c.) was warmed until a

clear solution was obtained and then kept overnight at room temperature. The solvent a unreacted diene were removed in a vacuum at 80°. The residual viscous liquid crystallis in the ice-chest and was drained on a tile and washed with water to remove maleic anhydric The product (0·6 g.; m. p. 47—49°) was recrystallised from light petroleum and gave imperfe needles of $\Delta^{4:10}$-*octahydronaphthalene*-1 : 2-*dicarboxylic anhydride* (VI; R = H), m.p. 52—5 (Found: C, 69·7; H, 6·7. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%). $\Delta^{4:10}$-*Octahydronaphthale* 1 : 2-*dicarboxylic acid*, formed by prolonged hydrolysis of the anhydride with hot wat crystallised from water in microscopic plates, m. p. 131—132·5° (Found: C, 64·5; H, 7·3 equiv., 114·2. $C_{12}H_{16}O_4$ requires C, 64·3; H, 7·2%; equiv., 112). A specimen of this acid whi had been dried in the air had m. p. 130—131° on rapid heating, but 157—158° (after sinterin on slow heating. The *diphenacyl* ester formed thin needles (from alcohol), m. p. 139·5—140 (Found: C, 72·85; H, 6·2. $C_{28}H_{28}O_6$ requires C, 73·0; H, 6·1%).

When $\Delta^{4:10}$-octahydronaphthalene-1 : 2-dicarboxylic acid or its anhydride was boil with sodium hydroxide solution, it was partly isomerised; acidification gave a *lactonic ac* which, in contrast to the dicarboxylic acid, was readily soluble in cold water; it crystallised fro benzene–ligroin in thin irregular plates, m. p. 176—176·5° (Found: C, 64·7; H, 7·3; equi 227·4. $C_{12}H_{16}O_4$ requires C, 64·3; H, 7·2%; equiv., 224). The *phenacyl* ester formed th plates (from aqueous alcohol), m. p. 131—131·5° (Found: C, 70·2; H, 6·4. $C_{20}H_{22}O_5$ requir C, 70·1; H, 6·5%); the m. p. was depressed 10° by admixture with the diphenacyl ester of t dicarboxylic acid.

1 : 4-*Diketodecahydrophenanthrene* (VII).—1-Vinyl-$\Delta^1$-*cyclo*hexene (0·9 g.) was added to solution of *p*-benzoquinone (0·6 g.) in methyl alcohol (8 c.c.), and the solution kept overnig at room temperature and then boiled for 2 hours. The oil precipitated by addition of wat solidified when cooled in a freezing mixture and was twice crystallised from methyl alcoh The *diketone* (VII) formed pale yellow, tabular crystals, m. p. 84—85·5°, which darkened standing (Found: C, 77·8; H, 7·6. $C_{14}H_{18}O_2$ requires C, 77·7; H, 7·45%).

9 : 10-*Diketo-octadecahydro*-1 : 2 : 5 : 6-*dibenzanthracene* (VIII).—A mixture of 1-vinyl-$\Delta$ *cyclo*hexene (1·2 g.), *p*-benzoquinone (0·5 g.), and tetralin (5 c.c.) was boiled under reflux f 10 minutes and then cooled. The resulting crystals were collected, washed with light petroleu and recrystallised from toluene. The *diketone* (VIII) (0·4 g. obtained from 3·7 g. of diene) form colourless needles, m. p. 200—203° (decomp.) (Found: C, 81·4; H, 8·7. $C_{22}H_{28}O_2$ requir C, 81·4; H, 8·7%). For dehydrogenation this diketone (45 mg.) was heated at 300—320° f 3 hours with platinum-black (30 mg.) and the sublimate was crystallised from benzene. T resulting yellowish leaflets had m. p. 257—258°, not depressed by 1 : 2 : 5 : 6-dibenzanthracer and gave a picrate, m. p. 212—213° (lit., 212°).

2-*Methyl*-1-*ethinyl*cyclo*hexanol*.—This was prepared, by the procedure used by Pinkn *et al.* (*loc. cit.*) for the preparation of 1-ethinyl*cyclo*hexanol, from 2-methyl*cyclo*hexanone (28 g ether (100 c.c.), potassium (10 g.), *tert.*-amyl alcohol (130 c.c.), and a saturated (at − 1 ethereal solution of acetylene (100 c.c.). After two distillations the resulting carbinol (22 had b. p. 88—96°/33 mm. For analysis, a portion was repeatedly fractionated, and then h b. p. 83—84°/21 mm. (Found: C, 77·0; H, 10·0. $C_9H_{14}O$ requires C, 78·2; H, 10·2%). *Methyl*-1-*ethinyl*cyclo*hexanol* formed a colourless mobile liquid with a camphor-like odou and did not crystallise on long standing. Its p-*nitrobenzoate* formed small tabular crysta (from methyl alcohol), m. p. 135—136° (Found: C, 66·95; H, 6·0. $C_{16}H_{17}O_4N$ requires 66·9; H, 6·0%), and its 3 : 5-*dinitrobenzoate* formed colourless microscopic plates (from aqueo alcohol), m. p. 76·5—79° (Found: C, 57·8; H, 4·9. $C_{16}H_{16}O_6N_2$ requires C, 57·8; H, 4·85%

2-*Methyl*-1-*vinyl*cyclo*hexanol*.—A solution of the foregoing carbinol (16·5 g.) in alcoh (200 c.c.) was shaken with hydrogen in presence of palladium-black (0·3 g.) until 3 l. had bee absorbed at 23° and 767 mm. The resulting 2-*methyl*-1-*vinyl*cyclo*hexanol* (12·9 g.) formed colourless mobile liquid, b. p. 86·5—90°/30 mm. (Found: C, 76·1; H, 11·3. $C_9H_{16}O$ requir C, 77·1; H, 11·5%). Its p-*nitrobenzoate* formed small thin plates (from aqueous methyl alcohol m. p. 71—72° (Found: C, 66·1; H, 7·0. $C_{16}H_{19}O_4N$ requires C, 66·4; H, 6·6%), and i 3 : 5-*dinitrobenzoate* formed small thin plates (from alcohol), m. p. 120—120·5° (Found: 57·25; H, 5·7. $C_{16}H_{18}O_6N_2$ requires C, 57·5; H, 5·4%).

2-*Methyl*-1-*ethyl*cyclo*hexanol* was prepared for comparative purposes, the following procedu giving a very much better yield than that of Murat (*Ann. Chim.*, 1909, 16, 116): A solutic of 2-methyl*cyclo*hexanone (18 g.) in ether (50 c.c.) was added to a mechanically stirred Grignar solution prepared from ethyl iodide (25 g.), magnesium (4·2 g.), and ether (170 c.c.), cooled t 0°. After being kept in the ice-bath for ½ hour, the mixture was allowed to warm to roo temperature, then boiled for an hour, and finally kept overnight at room temperature. Th

roduct was decomposed with ice-cold ammonium chloride solution, and the washed ethereal ıyer was shaken for 2 hours with saturated sodium bisulphite solution to remove unreacted ctone. The ethereal solution was washed, dried (sodium sulphate), and distilled, yielding 7·3 g. (75% yield) of 2-methyl-1-ethyl*cyclo*hexanol, b. p. 81—84°/23 mm. Its 3 : *5-dinitro-nzoate* formed thin irregular plates (from aqueous alcohol), m. p. 105·5—107·5° (Found : , 56·9; H, 6·2. $C_{16}H_{20}O_6N_2$ requires C, 57·1; H, 6·0%). A crystalline *p*-nitrobenzoate ould not be obtained.

1-*Methyl*-2-*vinyl*-$\Delta^1$-cyclo*hexene*.—2-Methyl-1-vinyl*cyclo*hexanol (1·4 g.), purified through s *p*-nitrobenzoate, was heated for an hour at 180—185° with potassium hydrogen sulphate ·5 g.) in an atmosphere of nitrogen. The resulting 1-*methyl*-2-*vinyl*-$\Delta^1$-cyclo*hexene* formed colourless mobile liquid, b. p. 156—157° (Found : C, 86·7; H, 12·1. $C_9H_{14}$ requires C, 88·45; , 11·55%).

9-*Methyl*-$\Delta^{4:10}$-*octahydronaphthalene*-1 : 2-*dicarboxylic Anhydride* (VI; R = Me).—The foresaid diene (6·2 g.), prepared by dehydration of the crude distilled carbinol (8·3 g.), was dded to a mixture of maleic anhydride (5 g.) and xylene (10 c.c.), and the solution heated at 0° for ½ hour and then kept overnight at room temperature. The adduct partly crystallised nd more was isolated from the liquors by vacuum concentration. After washing with water remove maleic anhydride, 9-methyl-$\Delta^{4:10}$-octahydronaphthalene-1 : 2-dicarboxylic anhydride /I; R = Me) crystallised from ligroin in thin irregular plates, m. p. 114—114·5° (Meggy and obinson, *loc. cit.*, give 111·5°) (Found : C, 70·9; H, 7·4. Calc. for $C_{13}H_{16}O_3$ : C, 70·9; H, 3%). The same anhydride resulted when the purified diene was allowed to react with maleic nhydride in benzene at room temperature for 48 hours. The acid obtained by aqueous or kaline hydrolysis of the anhydride crystallised from water in microscopic prisms, m. p 179—31° (Meggy and Robinson give 171°) (Found : C, 65·4; H, 7·7. Calc. for $C_{13}H_{18}O_4$ : C, 65·5; , 7·6%).

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## 16. *Isomorphous Relationships of Some Analogous Organic Derivatives of Oxygen, Sulphur, and Selenium.*

By N. M. CULLINANE and C. A. J. PLUMMER.

Observations of temperature–concentration diagrams of binary mixtures of (a) diphenylene oxide, sulphide, and selenide, and (b) diphenylene dioxide, disulphide, and diselenide, have been made. The results are in harmony with the periodic relationships of the elements oxygen, sulphur, and selenium. For instance, in the former series it has been found that diphenylene sulphide and selenide and diphenylene oxide and sulphide yield continuous series of solid solutions, while diphenylene oxide and selenide exhibit only partial solid solubility.

The system diphenylene disulphide–diselenide shows that an unbroken series of solid solutions is present, whereas the systems diphenylene dioxide–disulphide and diphenylene dioxide–diselenide exhibit eutectics with negligible solid solution formation.

The spatial configurations of the molecules are discussed in the light of the above results.

IIS work was undertaken in order to ascertain if the isomorphous relationships of ıalogous derivatives of oxygen, sulphur, and selenium are in harmony with the periodic lationships of these elements. The series investigated were the following diphenylene rivatives: (*a*) oxide, sulphide, and selenide, and (*b*) dioxide, disulphide (thianthren), ıd diselenide (selenanthren), and the ability of binary mixtures of these compounds to rm solid solutions was chosen as the criterion of isomorphism.

The only recorded investigation of this type is due to Pascal (*Bull. Soc. chim.*, 1912, , 1030), who carried out similar experiments with diphenyl oxide, sulphide, and

selenide. Of these substances, however, the last is unstable, and the purity of t specimen employed is in doubt (Drew and Landquist, J., 1935, 1482), whereas t compounds herein described are all quite stable, can be satisfactorily purified, a crystallise well.

Although recent investigations indicate that chemically dissimilar compounds n exhibit isomorphism provided that the shape of the space occupied by the molecule similar (see, *e.g.*, Grimm, Günther, and Tittus, *Z. physikal. Chem.*, 1931, *B*, **14**, 1 Pirsch, *Ber.*, 1936, **69**, 1323; Lettré, Barnbeck, and Lege, *ibid.*, p. 1151), neverthel substances of analogous chemical constitution possess geometrically similar molecules virtue of this chemical similarity, and hence it may be concluded that the types of ph diagrams obtained in a series of compounds such as those now described are related the chemical constitutions of the compounds.

Pascal's results (*loc. cit.*) show that, although diphenyl sulphide and selenide giv *continuous series of solid solutions* (type III, Roozeboom, *Z. physikal. Chem.*, 1899, 385), only limited solid solubility is exhibited by diphenyl oxide and sulphide (type and by diphenyl oxide and selenide (type V).

That the spatial structures of the diphenyl oxide and sulphide molecules are dissim is shown by the different values of the oxygen and sulphur valency angles in tl compounds: Sutton and Hampson (*Trans. Faraday Soc.*, 1935, **31**, 945), fron consideration of electrical dipole-moment measurements, conclude that these angles $128° \pm 4°$ and $113° \pm 3°$ respectively. The value of the selenium valency angle diphenyl selenide is not known, but Pascal's results indicate that it is not far remo from that of the sulphur angle in diphenyl sulphide.

In the series diphenylene oxide, sulphide, selenide, the heterocyclic atoms form of a rigid system in which therefore the oxygen, sulphur, and selenium valency an probably differ less than in the corresponding diphenyl derivatives. The results s that diphenylene sulphide and selenide yield solid solutions in all proportions (Fig type I), as also do diphenylene oxide and sulphide (Fig. 1; type III), while dipheny oxide and selenide possess limited solid solubility only (Fig. 3; type V). The cl resemblance between sulphur and selenium than between oxygen and selenium is confirmed.

The results obtained for the system diphenylene oxide–sulphide indicate a simil in space structure agreeing with information furnished by dipole-moment measurem The moment of furan is very small (*ca.* 0·65 D.; Hunter and Partington, J., 1931, 2 Smyth and Walls, *J. Amer. Chem. Soc.*, 1932, **54**, 3234), and that of diphenylene c (dibenzofuran) is roughly of the same order (0·9; Bretscher, *Helv. Physica Acta*, 192 257), from which it may be inferred that the three rings in the latter compounc approximately coplanar, for any pronounced bending of the molecule, such as occurs, in thianthren (Bennett and Glasstone, J., 1934, 128), would result in a conside increase in the value of the moment. Thiophen and diphenylene sulphide (dib thiophen) present an analogous case. The moment of the former is *ca.* 0·6 (Hassel Næshagen, *Tidsskr. Kjemi*, 1930, **10**, 81), and that of the latter is also not far rem from zero (Bergmann and Tschudnowsky, *Z. physikal. Chem.*, 1932, *B*, **17**, 107). dipole moments of selenophen and diphenylene selenide (dibenzoselenophen) are unkr but the fact that diphenylene sulphide and selenide yield solid solutions in all propor suggests that the molecules of these two compounds are similar in spatial configurati

In the series diphenylene dioxide, disulphide, diselenide, we find that the last compounds yield a continuous series of solid solutions (Fig. 5; type I), wherea systems diphenylene dioxide–disulphide (Fig. 4) and –diselenide (Fig. 6) reveal a eu in each case with negligible solid-solution formation. The strong resemblance bet sulphur and selenium and their dissimilarity to oxygen is thus confirmed. The ab of solid-solution formation in the first pair of the series is no doubt connected wit considerable difference in the spatial configurations of the molecules. Diphen dioxide has zero dipole moment (Bennett, Earp, and Glasstone, J., 1934, 1180), sc the molecule must be planar, and consequently the oxygen valency angles cannot b than 120°, whereas in the case of the disulphide, the moment of which is 1·5 (Bennet

asstone, *loc. cit.*; cf. Bergmann, *Ber.*, 1932, **65**, 463), the molecule is folded along a line ssing through the sulphur atoms, and therefore the sulphur valency angles must be less an 120°. Although the dipole moment of diphenylene diselenide has not been termined, the evidence furnished by the present work indicates that its molecule also ssesses a folded structure akin to that of thianthren.

The molecular volumes of thianthren and selenanthren were found to be very similar, d the close similarity of these compounds was further confirmed by crystallographic easnrements (see p. 67).

EXPERIMENTAL.

*Purification of Materials.*—Some difficulty was experienced in preparing a sample of henylene oxide of sufficient purity for our purpose. A satisfactory specimen was finally tained by fractional distillation, followed by three recrystallisations from dilute alcohol, d then two sublimations; it formed colourless scales, m. p. 82·4°.

Diphenylene sulphide was recrystallised from alcohol, then sublimed, and again similarly rystallised; colourless needles, m. p. 98·9°. The selenide was recrystallised from alcohol, blimed, and then distilled with steam. Further recrystallisation from alcohol afforded ourless needles, m. p. 71·0°.

Diphenylene dioxide, purified by distillation with steam, recrystallisation (twice) from ohol, and finally sublimation, formed long, thin, colourless needles, m. p. 119·7°. The ulphide was distilled under diminished pressure, followed by sublimation and recrystallisation rice) from acetone; the pure product consisted of colourless needles, m. p. 156·7°. rification of diphenylene diselenide was effected by distillation under reduced pressure, owed by repeated recrystallisation from acetone; colourless needles, m. p. 179·4°.

*Method of Experiment.*—Thaw points ($T_1$) and melting temperatures ($T_2$) were determined the method of Rheinboldt and Kircheisen (*J. pr. Chem.*, 1925, **111**, 246; 1926, **113**, 348), determinations being carried out in small capillaries. Temperatures were recorded on a all Anschütz thermometer graduated to 0·1°, which had been standardised at the National ysical Laboratory. For each system investigated determinations of $T_1$ and $T_2$ were made ler exactly similar conditions. Values of $T_1$ could be reproduced to within 0·2°, and those $T_2$ to within a narrower range. For the pure compounds, $T_1$ and $T_2$ did not differ by more n 1°.

The results are shown graphically in Figs. 1—6, and the complete data are tabulated below.

*System Diphenylene Oxide–Diphenylene Sulphide (Fig. 1).*

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| hide, mols. % ........... | 0 | 8·1 | 13·5 | 23·2 | 41·6 | 49·9 | 66·7 | 84·2 | 100 |
| ................................ | 81·7° | 81·1° | 80·8° | 80·4° | 80·6° | 81·5° | 83·3° | 88·0° | 98·4° |
| ................................ | 82·4 | 81·9 | 81·1 | 80·6 | 81·4 | 82·5 | 85·6 | 91·6 | 98·9 |

The curve is very unusual, inasmuch as the maximum depression of the m. p. is only 1·8°, esponding to 26 mols. % of sulphide.

*System Diphenylene Sulphide–Diphenylene Selenide (Fig. 2).*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| hide, mols. % ........... | 0 | 7·6 | 19·9 | 48·1 | 76·0 | 85·6 | 100 |
| ................................ | 70·0° | 70·1° | 71·0° | 75·2° | 83·2° | 87·5° | 98·4° |
| ................................ | 71·0 | 72·2 | 75·9 | 85·0 | 94·0 | 95·7 | 98·9 |

The m. p.'s of all mixtures lie between those of the pure components.

*System Diphenylene Oxide–Diphenylene Selenide (Fig. 3).*

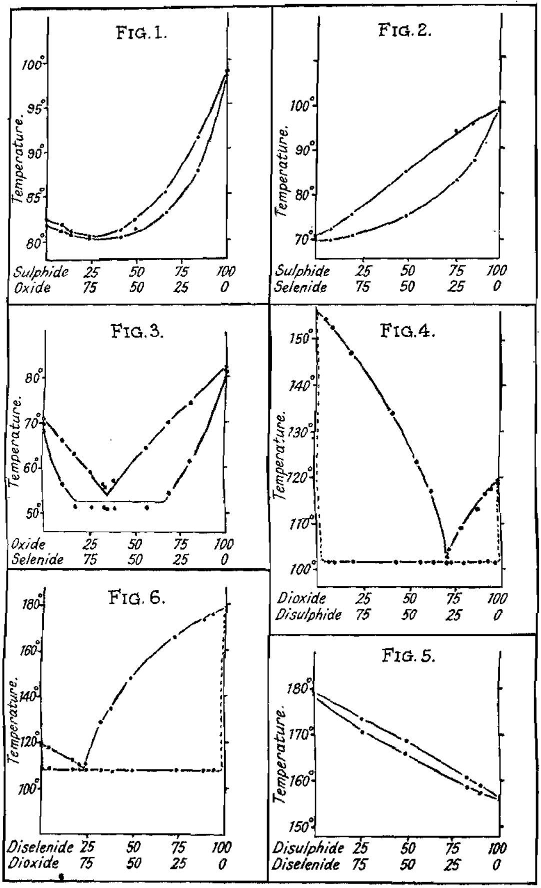
| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| le, mols. % | 0 | 10·2 | 17·3 | 26·1 | 32·7 | 34·1 | 39·2 | 57·0 | 69·2 | 80·8 | 100 |
| .............. | 70·0° | 56·2° | 51·8° | 51·7° | 51·6° | 51·0° | 51·3° | 51·7° | 54·9° | 61·8° | 81·7° |
| .............. | 71·0 | 66·1 | 63·8 | 59·5 | 56·6 | 56·0 | 57·7 | 64·9 | 70·2 | 74·6 | 82·4 |

The system reveals a eutectic at 53°, corresponding to 35 mols. % of oxide, the com- tions of the solid solutions being *ca.* 15 and 63 mols. % of oxide.

*System Diphenylene Dioxide–Diphenylene Disulphide (Fig. 4).*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ide, mols. % ...... | 0 | 5·2 | 9·0 | 19·3 | 42·3 | 56·0 | 63·1 |
| ........................ | 156·1° | 101·[illegible]° | 101·8° | 101·8° | 101·6° | 101·6° | 101·6° |
| ........................ | 156·7 | 154·7 | 153·0 | 147·8 | 134·2 | 123·8 | 117·2 |
| ide, mols. % ...... | 71·1 | 72·2 | 78·9 | 87·7 | 92·6 | 96·0 | 100 |
| ........................ | 101·7° | 101·7° | 101·6° | 101·9° | 101·8° | 101·5° | 118·8° |
| ........................ | 102·8 | 104·7 | 109·9 | 113·8 | 116·2 | 117·7 | 119·7 |

The curve shows a simple eutectic, with no solid solution formation. The eutectic poin is 101·6°, corresponding to 69·5 mols. % of dioxide.




*Legends to abscissæ give mols. %.*

*System Diphenylene Disulphide–Diphenylene Diselenide (Fig. 5).*

| | | | | | | |
|---|---|---|---|---|---|---|
| Disulphide, mols. % | 0 | 25·6 | 49·1 | 81·9 | 89·3 | 100 |
| $T_1$ | 178·8° | 170·6° | 166·0° | 159·0° | 157·8° | 156·1° |
| $T_2$ | 179·4 | 173·7 | 168·8 | 161·0 | 159·2 | 156·7 |

The m. p.'s of all mixtures lie between those of the pure components.

The densities and molecular volumes are as follows: Disulphide, $d = 1{\cdot}43$, mol. vol. = 151. ;elenide, $d = 1{\cdot}92$, mol. vol. = 160.

Both solids crystallise in the monoclinic system, the axial ratios and angle being as follows ivate communication from Messrs. R. G. Wood and J. E. Crackston of the Physics partment of this College):

Disulphide, $a : b : c = 2{\cdot}34 : 1 : 2{\cdot}47$; $\beta = 132° 22'$.

Diselenide, $a : b : c = 2{\cdot}40 : 1 : 2{\cdot}53$; $\beta = 132° 59'$.

A complete crystallographic and *X*-ray study of these substances will be published ;where.

*System Diphenylene Dioxide–Diphenylene Diselenide* (*Fig.* 6).

| | | | | | | |
|---|---|---|---|---|---|---|
| elenide, mols. % .............. | 0 | 2·9 | 16·6 | 20·4 | 23·8 | 32·1 |
| ........................................ | 118·8° | 108·4° | 108·1° | 108·1° | 108·0° | 108·0° |
| ........................................ | 119·7 | 118·7 | 112·5 | 110·5 | 111·2 | 129·6 |
| elenide, mols. % .............. | 38·3 | 49·5 | 73·3 | 88·3 | 93·6 | 100 |
| ........................................ | 107·9° | 108·2° | 108·2° | 108·2° | 108·3° | 178·8° |
| ........................................ | 135·8 | 148·6 | 167·0 | 174·5 | 176·6 | 179·4 |

The system forms a simple eutectic at 108·2°, with no solid solution formation, corresponding 77 mols. % of dioxide.

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TATEM LABORATORIES, UNIVERSITY COLLEGE, CARDIFF. [*Received, November 6th*, 1937.]

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## 17. *Solubility Influences. Part V. The Influence of Aliphatic Alcohols on the Solubility of Ethyl Acetate in Water.*

By D. G. BEECH and S. GLASSTONE.

The three-component systems consisting of water, ethyl acetate, and each of the following alcohols: methyl, ethyl, *n*- and *iso*-propyl, *n*-, *iso*-, *sec*.- and *tert*.-butyl, have been studied at 0° and 20°. In each case a number of the conjugate solutions, *i.e.*, aqueous and ester layers, were examined and their compositions determined; from the results the distribution ratio of ethyl acetate between the two layers was calculated. The addition of small amounts of alcohol to water appears to decrease the solubility of ethyl acetate, especially at low temperatures, but the effect is due to the decrease in activity (concentration) of the ethyl acetate in the ester layer because of the presence of appreciable amounts of alcohol. The distribution ratio is a corrected solubility which allows for the change in activity and shows no such decrease. By plotting the distribution ratio against the molecular ratio of alcohol to water in the aqueous layer, curves are obtained showing the influence on the corrected solubility of ethyl acetate of replacing water molecules by an equal number of molecules of alcohol. In this way the relative effects of the different alcohols can be compared and discussed. Four main factors are shown to affect the solubility of ethyl acetate in alcohol–water mixtures. At low concentrations of alcohol, complex formation between ester and water and its modification due to depolymerisation of the water by the alcohol is most important, but as the concentration is increased, first the relative areas of the non-polar and polar parts of the alcohol molecules and then their relative internal pressures become the dominant factors. Complex formation between alcohol and ester is shown by the results to have an unimportant influence on the solubility of ethyl acetate in aqueous-alcoholic solution.

'ER an investigation of the factors influencing the solubility of esters had been ımenced, Kendall (*Trans. Faraday Soc.*, 1937, 33, 2) gave an account of the freezing ıts of solutions of ethyl acetate in aqueous ethyl alcohol. From the data the clusion was drawn that, at low temperatures at least, ethyl alcohol diminishes the ıbility of ethyl acetate in water, and a tentative explanation of the surprising result proposed by one of us (Glasstone, *ibid.*, p. 8). In the course of experiments designed

to confirm the observations and to test the hypothesis, it became evident that the decrea of solubility was apparent rather than real. When excess of ethyl acetate is added water, the ester dissolves very little water and so the upper layer consists of almost pu ester, but if instead of water an aqueous alcohol is used, the upper layer may conta appreciable amounts of alcohol and water, with the result that the mol.-fraction of est is reduced considerably below unity. This is particularly the case with the high alcohols which have a limited solubility in water yet are completely miscible with eth acetate. The decrease in solubility of the ester in the aqueous layer found under the conditions is not remarkable, since the ethyl acetate with which it is in equilibrium is a much lower activity than in the pure state. It was clear, therefore, that reliab information on the influence of alcohols on the solubility of ethyl acetate in water cou only be obtained by a complete investigation, involving the analysis of both liquid layer for a series of alcohols over a range of concentrations.

For this reason the liquid-phase equilibria in the three-component systems, co sisting of water, ethyl acetate, and an alcohol were studied at 0° and 20°, and the resul plotted on triangular diagrams. In each case a number of tie-lines, joining the poin giving the compositions of the conjugate layers, were determined. The results obtain with methyl, ethyl, *n*- and *iso*-propyl, and *n*-, *iso*-, *sec.*-, and *tert.*-butyl alcohols are no described and discussed.

## Experimental.

*Materials.—Ethyl acetate.* In the preliminary experiments three different products we employed: (i) A quantity of the ester was prepared from glacial acetic acid and absolu alcohol by Roberts's method (*J. Soc. Chem. Ind.*, 1924, **43**, 295T); it was dried over anhydrou potassium carbonate, refluxed several times with fresh portions of phosphoric oxide, and the fractionated over a small quantity of the latter substance. The fraction of b. p. 77·0–77·2°/760 mm. was collected. (ii) A good commercial specimen was kept over calcium chloric and distilled, the portion coming over between 74° and 78° being collected. This was treated wit phosphoric oxide and fractionated as described above. (iii) A similar specimen was wash three times with an equal volume of half-saturated sodium chloride solution and twice wit water; it was then stood over calcium chloride and fractionally distilled. A number solubility determinations in water were made with the three products described, and in eve case the results were the same within the limits of experimental error; expressed in g. of eth acetate per 100 g. of water, the solubilities were:

At 0°, 10·70 $\pm$ 0·05; at 20°, 8·40 $\pm$ 0·04; at 40°, 6·97 $\pm$ 0·04.

The value for 20° is in good agreement with that (8·42 g.) obtained by Schlesinger and Kubasow (*Z. physikal. Chem.*, 1929, **142**, *A*, 27), although most of the results in the literature show considerable variation. Since the specimens described above had almost identical solubilitie most of the measurements recorded in this paper were made with the third product.

*Alcohols.* Good commercial specimens were fractionated, and the portions distillin within a narrow range of the recorded b. p.'s were collected and used. The densities agree very closely with the best values found in the literature (*e.g.*, Butler *et al.*, J., **1933**, **674**; 193 280). *tert.*-Butyl alcohol was not distilled, but was cooled until partly frozen; the supernatar liquid was poured off, and the remaining solid retained.

*Method of Experiment.*—The data for the solubility curves were generally obtained by th synthetic method: known amounts of ethyl acetate and water were mixed and sufficient the appropriate alcohol was run in to make the system homogeneous. The addition of th alcohol was carried out very slowly and the temperature was kept constant, although th effect of a slight raising or lowering of temperature frequently proved useful as a test fo saturation. Many of the results were confirmed by analysis of the saturated solutions, th ester being determined in the usual manner by hydrolysis with alkali. To obtain the tie-line the general practice was to make up a mixture with known weights of the three component and to determine the amount of ethyl acetate in the upper layer by analysis. These dat together with the solubility curve, enable the position of the tie-line to be fixed. On accour of the shape of the curves, this method was found to be more reliable than determining th ester concentration of both liquid layers. Measurements were made at 0° and 20°.

*Results.*—The results obtained were plotted on triangular diagrams, portions of which ar shown in Figs. 1 and 2: all compositions are in terms of weight percentages. The data fo

ie conjugate ternary liquids, as obtained from the extremities of the tie-lines, are given in able I.

FIG. 1.

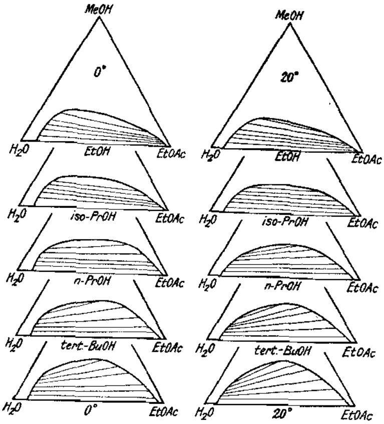
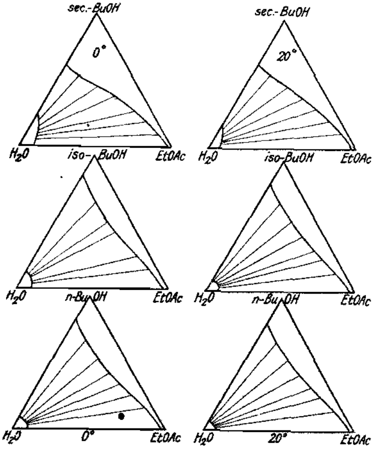



FIG. 2.




In order to see more clearly the significance of the results in Table I, the distribution ratios thyl acetate between the aqueous and the ester layer, with concentrations expressed in

TABLE I.

*Compositions of conjugate solutions expressed as weight %.*

| Temp. 0°. | | | | | | Temp. 20°. | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $H_2O$. | EtOAc. | ROH. | $H_2O$. | EtOAc. | ROH. | $H_2O$. | EtOAc. | ROH. | $H_2O$. | EtOAc. | ROH. |
| 90·4 | 9·6 | 0·0 | 2·3 | 97·7 | 0·0 | 92·2 | 7·8 | 0·0 | 2·8 | 97·2 | 0· |
| | | | | | Methyl alcohol. | | | | | | |
| 85·4 | 9·5 | 5·1 | 2·6 | 97·1 | 0·3 | 87·8 | 8·0 | 4·2 | 3·4 | 95·6 | 1· |
| 80·8 | 9·5 | 9·7 | 3·2 | 95·5 | 1·3 | 83·0 | 8·4 | 8·6 | 4·3 | 92·6 | 3·1 |
| 75·5 | 10·2 | 14·3 | 3·7 | 94·1 | 2·2 | 79·0 | 9·3 | 11·7 | 5·8 | 88·9 | 5· |
| 72·0 | 11·2 | 16·8 | 4·8 | 91·1 | 3·9 | 74·6 | 10·5 | 15·0 | 6·3 | 87·4 | 6· |
| 60·4 | 16·3 | 23·3 | 7·9 | 84·4 | 7·7 | 65·2 | 14·5 | 20·3 | 10·2 | 79·8 | 10· |
| | | | | | | 55·1 | 21·4 | 23·5 | 15·0 | 71·3 | 13· |
| | | | | | Ethyl alcohol. | | | | | | |
| 86·9 | 9·3 | 3·8 | 2·4 | 97·5 | 0·1 | 88·1 | 7·9 | 4·0 | 3·6 | 94·4 | 2· |
| 84·2 | 9·1 | 6·7 | 2·9 | 95·6 | 1·5 | 84·0 | 8·4 | 7·6 | 5·3 | 89·2 | 5· |
| 80·2 | 9·0 | 10·8 | 3·6 | 93·1 | 3·3 | 80·4 | 9·2 | 10·4 | 7·0 | 85·2 | 7· |
| 76·9 | 9·2 | 13·9 | 4·6 | 89·6 | 5·8 | 75·6 | 10·7 | 13·7 | 8·6 | 81·2 | 10· |
| 73·8 | 9·7 | 16·5 | 6·7 | 84·1 | 9·2 | 70·5 | 13·0 | 16·5 | 13·4 | 72·1 | 14· |
| 68·9 | 11·3 | 19·8 | 10·7 | 75·9 | 13·4 | 62·6 | 17·9 | 19·5 | 21·3 | 60·4 | 18· |
| | | | | | *iso*Propyl alcohol. | | | | | | |
| 87·0 | 9·0 | 4·0 | 3·0 | 96·2 | 0·8 | 88·7 | 7·9 | 3·4 | 4·2 | 91·7 | 4· |
| 83·6 | 8·8 | 7·6 | 4·4 | 89·9 | 5·7 | 84·8 | 8·5 | 6·7 | 5·8 | 86·6 | 7· |
| 81·4 | 8·7 | 9·9 | 5·8 | 85·4 | 8·8 | 82·0 | 9·2 | 8·8 | 8·4 | 79·8 | 11 |
| 77·5 | 8·7 | 13·8 | 9·3 | 76·2 | 14·5 | 78·2 | 10·0 | 11·8 | 12·3 | 71·3 | 16 |
| 73·9 | 9·3 | 16·8 | 16·0 | 63·3 | 20·7 | 74·0 | 11·4 | 14·6 | 18·8 | 59·4 | 21 |
| | | | | | | 69·5 | 13·7 | 16·8 | 26·6 | 48·3 | 25 |
| | | | | | *n*-Propyl alcohol. | | | | | | |
| 87·7 | 9·2 | 3·1 | 4·0 | 91·6 | 4·4 | 88·7 | 7·8 | 3·5 | 4·2 | 90·4 | 5 |
| 84·7 | 9·1 | 6·2 | 5·2 | 87·3 | 7·5 | 85·9 | 8·0 | 6·1 | 7·6 | 80·4 | 12 |
| 82·6 | 8·9 | 8·5 | 9·6 | 75·7 | 14·7 | 84·0 | 8·3 | 7·7 | 11·3 | 71·5 | 17 |
| 78·9 | 9·2 | 11·9 | 16·0 | 61·3 | 22·7 | 81·3 | 9·0 | 9·7 | 17·9 | 58·4 | 23 |
| 74·1 | 10·2 | 15·7 | 29·0 | 43·6 | 27·4 | 79·0 | 9·7 | 11·3 | 23·7 | 49·6 | 26 |
| | | | | | | 72·6 | 12·2 | 15·2 | 34·7 | 36·5 | 28 |
| | | | | | *tert*.-Butyl alcohol. | | | | | | |
| 87·5 | 8·8 | 3·7 | 3·2 | 94·1 | 2·7 | 88·9 | 7·6 | 3·5 | 5·0 | 88·9 | [illegible] |
| 84·6 | 8·4 | 7·0 | 5·3 | 85·1 | 9·6 | 86·8 | 7·5 | 5·7 | 7·7 | 79·4 | 12 |
| 82·3 | 8·0 | 9·7 | 6·9 | 79·5 | 13·6 | 84·3 | 7·4 | 8·3 | 11·4 | 68·0 | 2 |
| 80·5 | 7·8 | 11·7 | 12·0 | 66·1 | 21·9 | 81·5 | 7·7 | 10·8 | 17·4 | 54·2 | 2 |
| 78·0 | 7·7 | 14·3 | 17·4 | 55·9 | 26·7 | 79·8 | 7·8 | 12·4 | 22·6 | 45·5 | 3 |
| 76·2 | 7·8 | 16·0 | 25·0 | 43·7 | 57·3 | 75·5 | 8·8 | 15·7 | 35·7 | 30·5 | 3 |
| | | | | | *sec*.-Butyl alcohol. | | | | | | |
| 87·1 | 8·7 | 4·2 | 5·2 | 85·9 | 8·9 | 89·8 | 7·2 | 3·0 | 5·2 | 82·7 | 1 |
| 85·3 | 8·2 | 6·5 | 8·8 | 72·5 | 18·7 | 88·9 | 6·8 | 4·3 | 9·0 | 69·2 | 2 |
| 83·9 | 7·5 | 8·6 | 12·4 | 61·5 | 26·1 | 88·5 | 6·5 | 5·0 | 13·1 | 56·0 | 3 |
| 82·1 | 6·7 | 11·2 | 19·3 | 43·5 | 37·2 | 86·5 | 5·3 | 8·2 | 17·7 | 43·3 | 3 |
| 80·3 | 5·6 | 14·1 | 26·5 | 28·9 | 44·6 | 85·4 | 4·2 | 10·4 | 23·6 | 28·8 | 4 |
| 77·6 | 3·7 | 18·7 | 35·2 | 12·8 | 52·0 | 83·7 | 2·6 | 13·7 | 30·5 | 13·1 | 5 |
| | | | | | *iso*Butyl alcohol. | | | | | | |
| 88·8 | 8·5 | 2·7 | 5·6 | 80·6 | 13·8 | 90·8 | 7·3 | 1·9 | 6·5 | 79·4 | 1 |
| 88·1 | 7·7 | 4·2 | 8·9 | 67·5 | 23·6 | 90·6 | 6·9 | 2·5 | 9·5 | 65·6 | 2 |
| 87·1 | 5·7 | 7·2 | 14·4 | 43·4 | 42·2 | 89·9 | 6·3 | 3·8 | 11·4 | 57·0 | 3 |
| 87·1 | 4·9 | 8·0 | 15·7 | 34·6 | 49·7 | 90·0 | 4·8 | 5·2 | 14·2 | 42·7 | 4 |
| 86·9 | 3·0 | 10·1 | 16·6 | 18·5 | 64·9 | 90·3 | 3·6 | 6·1 | 16·2 | 30·1 | 5 |
| | | | | | | 91·1 | 2·0 | 6·9 | 17·7 | 15·0 | 6 |
| | | | | | *n*-Butyl alcohol. | | | | | | |
| 89·7 | 8·0 | 2·3 | 6·4 | 78·3 | 15·3 | 92·0 | 6·3 | 1·7 | 7·0 | 78·6 | 1 |
| 89·3 | 7·3 | 3·4 | 10·0 | 65·2 | 24·8 | 92·0 | 5·8 | 2·2 | 10·7 | 63·4 | 2 |
| 89·2 | 6·8 | 4·0 | 13·5 | 53·0 | 33·5 | 92·1 | 5·3 | 2·6 | 13·3 | 54·0 | [illegible] |
| 89·1 | 6·3 | 4·6 | 16·0 | 42·5 | 41·5 | 92·2 | 4·2 | 3·6 | 16·2 | 41·5 | 4 |
| 89·0 | 4·8 | 6·2 | 18·3 | 20·3 | 52·4 | 92·4 | 3·4 | 4·2 | 18·3 | 28·6 | [illegible] |
| 89·7 | 3·7 | 7·6 | 19·6 | 14·3 | 66·1 | 93·0 | 1·8 | 5·2 | 19·6 | 14·3 | [illegible] |

*l.-fractions*, have been plotted in Figs. 3 and 4 against the molecular ratio of alcohol to ter in the aqueous layer for various concentrations of alcohol. The distribution ratio may regarded as a corrected solubility which allows for the decrease in activity of the ethyl state in the ester layer; as an approximation this activity is assumed equal to the mol.-ction. The curves obtained permit of a direct comparison of the relative effects of different ohols; they show the influence on the corrected solubility of ethyl acetate of replacing ving proportions of the total number of water molecules by an equal number of molecules alcohol.

FIG. 3.

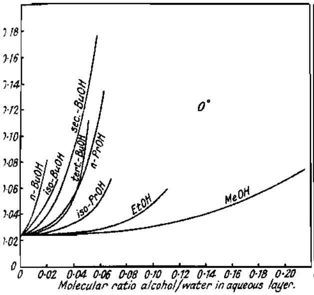
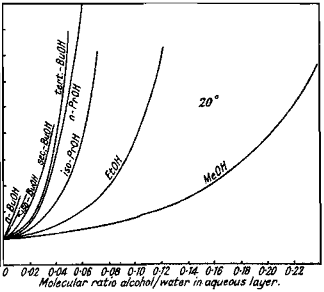



FIG. 4.




## DISCUSSION.

It will be seen from the curves in Figs. 3 and 4 that there is no evidence of a damental decrease in the solubility of ethyl acetate as a result of the addition of an ohol, although at low concentrations methyl and ethyl alcohols, especially, appear to little more effective than water as solvents in spite of the fact that they are miscible h ethyl acetate in all proportions. At higher concentrations, however, all the ohols bring about a large increase in the solubility of the ester, particularly at the her temperature.

There are at least four factors, dependent on the nature of the alcohol and on nperature, which will affect the solubility of ethyl acetate in a water–alcohol system: se will be considered in turn.

(*a*) The unexpectedly large solubility of ethyl acetate in water, the negative nperature coefficient, and the fact that the system is pseudo-ideal (Kendall and King, 1925, **127**, 1778) indicate that ester–water complexes, presumably involving a lrogen bond, are formed and these are the main cause of the relatively high solubility. ce liquid water is now generally regarded as virtually a large associated molecular ucture (Bernal and Fowler, *J. Chem. Physics*, 1933, **1**, 515; Sidgwick, *Ann. Reports*, 34, **31**, 42), it is probable that only free single molecules will be able to take part in the nplex formation with the ester. When an alcohol is added to water, there result, t, mutual depolymerisation [Jones and Murray, *Amer. Chem. J.*, 1903, **30**, 193; Jones l Veazey, *ibid.*, 1907, **37**, 405; see also Butler, Thomson, and Maclennan, J., 1933, (685)], and secondly, the formation of alcohol–water complexes, involving the simple lecules to a great extent. The former of these two effects, by producing more single ter molecules, will tend to bring about an increase in the solubility of ethyl acetate, the latter, which would be operative even if there were no depolymerisation, will rease the solubility because the alcohol will compete with the ester for the free water lecules. The net influence on the solubility of ethyl acetate will depend on the itive magnitudes of the two effects, of which some indication may be obtained from measurements of Young and Fortey (J., 1902, **81**, 717) on the thermal and volume

changes resulting when water and various alcohols are mixed. Since depolymerisatio will be accompanied by the absorption of heat, and probably an increase of volume whereas complex formation will have the opposite effects, it appears that the influenc of complex formation, which tends to lower the solubility of the ester, should be greatest with methyl alcohol but should become less as the hydrocarbon chain is lengthened. Although chain branching also favours compound formation, as shown by the existence of a stable solid hydrate of *tert.*-butyl alcohol, the thermal effect on mixing this alcohol with water suggests that there is considerable depolymerisation, and so the influence on solubility may not be marked. It may be noted that the conclusions drawn from thermal and volume changes are in agreement with those reached from general considerations, based on the probable influence of the electron-repelling tendencies of the alkyl groups and the size of the alcohol molecule on complex formation and depolymerisation.

Increase of temperature would be expected to decrease the concentration of alcohol–water complexes and possibly to increase the depolymerisation: hence the general effect of the operation of these factors would be in the direction of causing a relative increase in the solubility of ethyl acetate at 20° as compared with 0°.

(*b*) Since water and ethyl acetate are able to form a complex, it is reasonable to suppose that the ester will unite in an analogous manner with an alcohol, although to a smaller extent; evidence for this view has been obtained from infra-red absorption measurements on mixtures of methyl alcohol and esters (Williams and Gordy, *J. Amer. Chem. Soc.*, 1937, **59**, 817). The stability of the complexes is, however, probably not very great (cf. Merriman, J., 1913, **103**, 1774). The formation of such complexes probably involves a hydrogen bond between the alcohol and the ester, thus R·O·H · · · O<, consequently the presence of electron-repelling alkyl groups in the radical R of the alcohol should result in a decrease of stability. The effect of combination between ethyl acetate and the alcohol would be to increase the solubility of the ester, and this factor will evidently become less as the length and branching of the hydrocarbon chain of the alcohol are increased. Increase of temperature will decrease the extent of complex formation and any consequent influence on solubility will be diminished.

(*c*) The more the internal pressures of two liquids approximate to one another the greater will be their mutual solubility (Hildebrand, *J. Amer. Chem. Soc.*, 1916, **38**, 1452; "Solubility," 1936). Water and ethyl acetate have internal pressures which are markedly different, but the values for the alcohols, especially the butyl alcohols, are much closer to those of the ester. Although the internal pressure of a mixture of water and an alcohol is not exactly the mean of the values for the two constituents, nevertheless it will be much nearer to that of the ester than is the internal pressure of pure water (see Westwater, Frantz, and Hildebrand, *Physical Rev.*, 1928, **31**, 135): consequently, the ester should be more soluble in the alcohol–water mixture. The relative extents of the increase to be expected for the different alcohols may be assessed from their relative internal pressures: the values given below have been calculated by means of the formula $(280 + 24{\cdot}5t)/v$, where $t$ is the boiling point of the liquid on the Centigrade scale and $v$ the molar volume (see Hildebrand, *op. cit.*, p. 103). These may be compared with a figure of 73 for ethyl acetate.

*Relative internal pressures.*

| $H_2O$. | MeOH. | EtOH. | *n*-PrOH. | *iso*-PrOH. | *n*-BuOH. | *iso*-BuOH. | *sec.*-BuOH. | *tert.*-BuOH. |
|---|---|---|---|---|---|---|---|---|
| 429 | 161 | 116 | 94 | 88·5 | 80 | 78 | 76·5 | 71 |

is evident, therefore, that as far as internal pressure is concerned all the alcohols should enhance the solubility of ethyl acetate, the effect increasing approximately in the order given. Raising the temperature, however, might be expected to bring about a relatively greater increase of solubility for the lower alcohols, because the influence of internal pressure differences is diminished as the temperature is raised.

(*d*) The relative areas of the polar and non-polar portions of a molecule have some effect on its solubility (cf. Harkins, Brown, and Davies, *J. Amer. Chem. Soc.*, 1917, **39**, ; Langmuir, *Coll. Sym. Monographs*, 1925, **3**, 48; Butler, Thomson, and Maclennan, *cit.*, p. 681), and this factor may have some influence on the extent to which ethyl

acetate dissolves in the aqueous alcohol. Although ethyl acetate contains polar groupings, it behaves virtually as a non-polar substance from the standpoint of solubility, as seen for example by its complete miscibility with hexane; increasing the relative non-polar area of an alcohol should thus result in an increase of solubility. Increasing chain length should, therefore, have this effect, whereas branching of the chains would probably operate in the opposite direction.

An examination of the curves in Figs. 3 and 4 in the light of the above considerations shows that at small concentrations of alcohol, especially for the lower members of the series, complex formation between alcohol and water must be a very important factor, since in no other way is it possible to account for the increase in solubility of ethyl acetate being so small in the presence of these lower alcohols. That the same factor is effective with the higher alcohols, although generally masked by other influences which act in the opposite direction, is shown by the fact that the distribution ratio increases at first slowly with increasing alcohol concentration, and especially by the crossing of the curves for *n*-propyl and *tert.*-butyl alcohols at 0°. The greater tendency of the latter to form a complex with water molecules may account for this result; at 20°, where the extent of complex formation is diminished, the curves do not cross. Depolymerisation is, however, a factor of importance, especially with the higher alcohols; otherwise *tert.*-butyl alcohol would be expected to cause a much lower solubility than is actually observed, because of the stability of the alcohol–water complex which is probably much greater than that for ethyl alcohol. In fact, for the higher alcohols, depolymerisation is probably the dominating influence in determining the solubility of the ester in alcohol–water mixtures. Even for the lower alcohols, where the contributions of the internal pressure and relative polarity factors are probably small at low concentrations, the effect of alcohol–water complex formation cannot predominate, for otherwise the distribution ratio of ethyl acetate would fall below the value for water alone.

As the concentration of alcohol is increased it is evident that the other factors already discussed, all of which tend to increase the solubility of the ester, become more effective; of these, the formation of alcohol–ester complexes may be ruled out as being relatively unimportant, since its effect would decrease with increasing chain length. It is to be expected that the influence of the internal pressure and relative polarity factors should become more marked at higher alcohol concentrations, and these are probably responsible for the rapid rise in the distribution ratio. The former of these would lead to the solubilities of the ester in the alcohol–water mixtures containing the butyl alcohols increasing in the order $n < iso < sec. < tert.$, whereas the reverse is actually the case; this implies that the relative polarity, which would operate in the observed order, is the more effective. The direction of the curves for *tert.*- and *sec.*-butyl alcohols suggests that they would cross at very high concentrations, which are actually beyond the solubility limits, both at 0° and 20°; hence, under these conditions the internal pressure factor seems to become the more important.

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THE UNIVERSITY, SHEFFIELD 10. [*Received, December 8th,* 1937.]

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## 18. *The Dissociation Constant of Mandelic Acid in Water.*

By WILLIAM H. BANKS and CECIL W. DAVIES.

Conductivity measurements on aqueous solutions of sodium mandelate and mandelic acid at 24·915° lead to the value $K = 3{\cdot}88 \times 10^{-4}$ for the true dissociation constant of mandelic acid. The measurements on sodium mandelate were taken to fairly high concentrations, and show it to be a normal completely dissociated salt. Preliminary measurements on barium mandelate, however, yield low conductivities, and it is suggested that the solutions contain appreciable concentrations of the

intermediate ion, $C_6H_5\cdot CH(OH)\cdot CO\cdot OBa^{\cdot}$, for which a dissociation constant $K = 0{\cdot}17$ is derived. Some measurements of the adsorption of mandelic acid on a surface of paraffin wax are also described, and it is shown that conductivity measurements afford a sensitive method of studying adsorption at high dilutions.

THE measurements recorded in this paper were undertaken in 1930 with the primary object of testing the Debye–Hückel limiting activity equation, and their agreement with the requirements of this equation was reported in a preliminary note (*J. Amer. Chem. Soc.*, 1932, **54**, 1698). Since then, many investigations of a similar type (MacInnes and Shedlovsky, *ibid.*, p. 1429; Saxton and Langer, *ibid.*, 1933, **55**, 3638; Brockman and Kilpatrick, *ibid.*, 1934, **56**, 1483) have established the accuracy of the Debye–Hückel formula, so it is now unnecessary to stress this aspect of the work. In recording our results we have recalculated them to the basis of the new Jones and Bradshaw standard (*ibid.*, 1933, **55**, 1780).

The conductivity of the acid was measured in a cell of the Hartley and Barrett type. The cylindrical body of this was of transparent silica, but the cap and electrode leads were of borosilicate glass, and these were thinly coated with paraffin wax to avoid contact of the dilute acid solutions with a glass surface. Separate measurements of the adsorption of mandelic acid on paraffin wax enabled the necessary corrections to be calculated for the acid adsorbed on the leads of the cell.

## EXPERIMENTAL.

*Materials.*—The inactive mandelic acid was obtained from a commercial product by three recrystallisations from warm ether. Titration against standard baryta showed it to be $99{\cdot}9 \pm 0{\cdot}1\%$ pure acid. The lævorotatory acid was a pure specimen kindly placed at our disposal by Dr. J. Kenyon, F.R.S. Some difficulty was experienced in obtaining pure sodium mandelate. Its aqueous solubility is very high, and crystallisation from aqueous alcohol gives a product containing acid salt. A pure neutral product was obtained by mixing equivalent quantities of sodium hydroxide and mandelic acid in absolute alcohol and recrystallising from the same solvent. Barium mandelate was prepared from the pure acid and a slight excess of barium carbonate. After filtering and concentrating the solution, the salt was obtained as fine crystals of the hemihydrate (cf. MacKenzie, J., 1899, **75**, 964). The stability of these was not investigated; they were dried on filter-paper and used at once. The salt was analysed by the precipitation of barium sulphate [Found: Ba, 30·8. Calc. for $Ba(C_8H_7O_3)_2,\frac{1}{2}H_2O$: Ba, 30·6%].

Conductivity water was obtained from a still of the type described by Bourdillon (J., 1913, **103**, 791) and modified by Bengough, Stuart, and Lee (J., 1927, 2156). Owing to an error in the standard thermometer, which was not discovered until the measurements had been begun, the oil thermostat was maintained at $24{\cdot}915 \pm 0{\cdot}005°$.

*Conductivity Measurements on the Dilute Solutions.*—The apparatus was that described in an earlier paper (J., 1937, 432), and the technique employed was similar except that all measurements were made at a frequency of 1000 cycles; small corrections for polarisation were applied where necessary on the basis of the work just quoted, it being assumed (as sufficiently accurate for the purpose of these corrections) that the polarisation for a given cell is a function of the resistance only. The cell constant was determined by measurements on a number of dilute potassium chloride solutions at 17·915° and at 18·00°, the equation of the paper just cited and the temperature coefficients of Déguisne (see Kohlrausch and Holborn, "Leitvermögen der Elektrolyte," p. 199) being used; 17 determinations gave the mean value 0·047718, on the Jones and Bradshaw standard, with an average deviation of 0·02%.

*Sodium mandelate solutions.* Three series of measurements were made at 24·915°, and the results are in Table I. Col. 1 shows the concentration in g.-mol./l., calculated on a molecular weight of 174·056; the specific conductivity of the solvent water is given in col. 2, and that of the solution in col. 3.

*Mandelic acid solutions.* One run, which gave very discordant results, has been rejected. Of the remainder, recorded in Table II, the first two were on the inactive, and the third on the *l*-acid; for these runs the electrode leads were waxed, the area of wax being 44 sq. cm. The fourth run, on the inactive acid, was designed as a check on the adsorption corrections, and for this the whole interior of the cell was waxed, giving a total wax surface of 355 sq. cm. Col. 1 of the table shows the initial concentration of acid, col. 2 the true concentration after

TABLE I.

| $C \times 10^4$. | $\kappa_{soln.} \times 10^6$. | $\Lambda_1$. | $\Lambda_2$. | $C \times 10^4$. | $\kappa_{soln.} \times 10^6$. | $\Lambda_1$. | $\Lambda_2$. | $C \times 10^4$. | $\kappa_{soln.} \times 10^6$. | $\Lambda_1$. | $\Lambda_2$. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Run 1; $\kappa_{H_2O} = 0{\cdot}787 \times 10^{-6}$. | | | | Run 2; $\kappa_{H_2O} = 0{\cdot}671 \times 10^{-6}$. | | | | Run 3; $\kappa_{H_2O} = 0{\cdot}437 \times 10^{-6}$. | | | |
| 1·0091 | 8·652 | 77·95 | 78·80 | 1·0477 | 8·894 | 78·47 | 79·21 | 2·7385 | 21·757 | 77·85 | 78·20 |
| 2·2773 | 18·497 | 77·76 | 78·41 | 3·7467 | 29·774 | 77·68 | 78·13 | 5·2376 | 40·955 | 77·36 | 77·61 |
| 3·2195 | 25·785 | 77·65 | 78·25 | 5·7152 | 44·774 | 77·17 | 77·55 | 8·7830 | 67·946 | 76·86 | 77·06 |
| 4·4194 | 35·029 | 77·48 | 78·00 | 7·7594 | 60·397 | 76·97 | 77·30 | 10·931 | 84·116 | 76·55 | 76·72 |
| 5·4816 | 43·120 | 77·23 | 77·69 | 8·7246 | 67·692 | 76·82 | 77·15 | | | | |
| 7·5202 | 58·618 | 76·90 | 77·30 | 10·941 | 84·443 | 76·56 | 76·85 | | | | |

allowance had been made for adsorption. These corrections were obtained by interpolation from a curve, based on the data given in the next section, in which the amount of acid adsorbed per sq. cm. of wax surface was plotted against the equilibrium concentration of the solution. The corrections are very important for the fourth run, and the good agreement between this and the others shows that adequate allowance has been made for adsorption. Col. 3 gives the equivalent conductivity, calculated from the specific conductivity of the solution (without solvent correction) and the true concentrations of col. 2.

TABLE II.

| $C' \times 10^4$. | $C \times 10^4$. | $\Lambda$. | $C' \times 10^4$. | $C \times 10^4$. | $\Lambda$. |
|---|---|---|---|---|---|
| Run 1. Inactive acid. | | | Run 3. Active acid. | | |
| 13·198 | 13·190 | 158·65 | 5·7064 | 5·7023 | 210·35 |
| 22·949 | 22·938 | 128·91 | 11·764 | 11·757 | 165·70 |
| 62·309 | 62·307 | 85·44 | 18·574 | 18·565 | 140·19 |
| | | | 26·122 | 26·110 | 122·72 |
| Run 2. Inactive acid. | | | 34·339 | 34·329 | 109·95 |
| 7·3821 | 7·3770 | 193·50 | Run 4. | Inactive acid. | Waxed cell. |
| 14·014 | 14·006 | 155·36 | | | |
| 21·464 | 21·454 | 132·39 | 1·1253 | 1·1149 | 306·69 |
| 29·058 | 29·045 | 117·44 | 2·2820 | 2·2647 | 268·29 |
| 41·418 | 41·414 | 101·50 | 3·6947 | 3·6703 | 239·09 |

*Adsorption Measurements.*—For the adsorption measurements a roll of paper was drawn through hot paraffin wax and rolled loosely round a glass rod, to which one end of the roll was secured. With one end of the glass rod held by a rubber bung, the roll hung loosely coiled inside a waxed cylinder, the total area of waxed surface being 1950 sq. cm. Between experiments, the cylinder and coil were soaked in dilute sodium hydroxide, washed with much water, conductivity water being used for the final washing, and dried, after removal of adhering droplets with filter-paper, with pure air. An acid solution was then made up in the conductivity cell in the usual way, and after its conductivity had been determined, a fixed volume (260 ml.) was transferred to the adsorption vessel and this was allowed to remain in the thermostat with gentle agitation for 2 hours, the conductivity of the solution then being redetermined. The results are in Table III, where $C$ is the original concentration and $\kappa_A$ the original specific conductivity; $\kappa_B$ is the specific conductivity after adsorption, and $C_e$ the corresponding concentration of the solution, which was read off from a large-scale curve connecting $\kappa_A$ and $C$. From these results the amount of acid adsorbed was calculated and is shown in col. 5 of the table as the number of g.-mols. adsorbed per sq. cm.

TABLE III.

| $C \times 10^4$. | $\kappa_A \times 10^4$. | $\kappa_B \times 10^4$. | $C_e \times 10^4$. | $\Gamma \times 10^9$. | $\Gamma_{calc.} \times 10^9$. |
|---|---|---|---|---|---|
| 0·7142 | 0·2304 | 0·2212 | 0·6720 | 0·563 | 0·552 |
| 1·800 | 0·4867 | 0·4683 | 1·721 | 1·06 | 1·08 |
| 2·685 | 0·6926 | 0·6704 | 2·590 | 1·27 | 1·35 |
| 3·440 | 0·8317 | 0·8085 | 3·314 | 1·68 | 1·54 |
| 4·116 | 0·9233 | 0·9095 | 3·913 | 1·71 | 1·65 |
| 5·522 | 1·1721 | 1·1518 | 5·387 | 1·80 | 1·85 |

*Conductivity Measurements on More Concentrated Solutions.*—For these, a pipette cell of the Washburn type was used, and the cell constant was determined by means of Parker and Parker's 0·01*D*-potassium chloride solution. Corrected to the Jones and Bradshaw standard, the mean of three determinations was 2·0794. The salt solutions were all made up separately by weight, and their concentrations were calculated from the densities given below, which were determined in a small pycnometer; *m* is here the concentration in g.-mol./l. At higher

concentrations of sodium mandelate the measurements given in International Critical Tables, Vol. III, p. 84, were available.

*Densities of mandelate solutions at* 24·915°.

| | Sodium mandelate. | | | | Barium mandelate. | | |
|---|---|---|---|---|---|---|---|
| *m* | 0·0136 | 0·0236 | 0·0382 | *m* | 0·0215 | 0·0309 | 0·0534 |
| *d* | 0·9880 | 0·9987 | 0·9998 | *d* | 1·0025 | 1·0046 | 1·0104 |

The conductivity measurements are in Table IV, where col. 1 gives the concentrations in g.-equiv./l., and col. 2 the equivalent conductivities; in calculating these, a solvent correction of $1 \times 10^{-6}$ r.o. has been deducted.

TABLE IV.

| (*a*) Sodium mandelate at 24·915°. | | | | | | (*b*) Barium mandelate at 24·915°. | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| *C*. | Λ. | Λ, calc. | *C*. | Λ. | Λ, calc. | *C*. | Λ. | Λ, calc. | $(1-\alpha)$. | *K*. |
| 0·009776 | 72·35 | 72·35 | 0·02422 | 69·32 | 69·00 | 0·04302 | 64·83 | 68·93 | 0·100 | 0·176 |
| 0·01465 | 70·98 | 70·95 | 0·04676 | 66·13 | 66·09 | 0·06176 | 61·06 | 66·36 | 0·132 | 0·173 |
| 0·01932 | 70·00 | 69·94 | 0·09337 | 62·05 | 62·17 | 0·10685 | 54·74 | 61·85 | 0·196 | 0·175 |

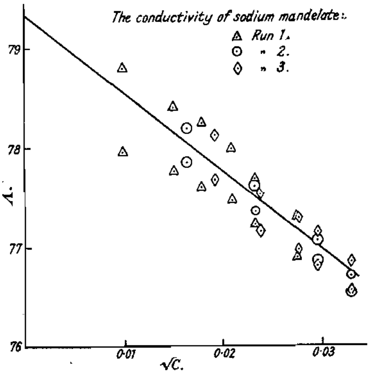
## DISCUSSION OF RESULTS.

*Adsorption Measurements.*—The experiments show that mandelic acid is very readily adsorbed on a paraffin-wax surface. The results can be expressed fairly well by the equation $1/\Gamma = 0{\cdot}359 \times 10^9 + 1{\cdot}03 \times 10^5 \times 1/C_e$; values calculated from this formula are shown in the last column of Table III. From Langmuir's derivation of this equation, the reciprocal of the limiting value $0{\cdot}359 \times 10^9$, *i.e.*, $2{\cdot}78 \times 10^{-9}$, should represent the number of g.-mols. of acid per cm.² necessary to form a complete unimolecular layer, and it will be seen from the table that if this is approximately true, adsorption has already reached one-half of this saturation value at a concentration of 0·0003N. The wax surface was by no means smooth, and if *n* represents the factor by which the measured surface must be multiplied to give the actual surface, then the area occupied by one molecule of acid in the complete unimolecular layer is $n/2{\cdot}78 \times 10^{-9} \times 6{\cdot}06 \times 10^{23} = 5{\cdot}9 \times 10^{-16} \times n$ cm.², a reasonable value.

With a slightly more elaborate technique the accuracy of the measurements could readily have been increased, and we believe that interesting results would be obtained by applying the method to study the adsorption of electrolytes on various crystalline or other surfaces of limited area.

*Conductivity Measurements.*—The measurements on very dilute sodium mandelate solutions were undertaken to provide a value for the mobility of the mandelate ion, and they were also designed to test the combined solvent and hydrolysis correction put forward and used in previous papers (*Trans. Faraday Soc.*, 1932, **28**, 607; *Nature*, 1933, **131**, 328). The idea underlying this correction is that when the salt of a weak acid is dissolved in any but the purest water, the main interaction in dilute solutions is that expressed by the equation $A' + H_2CO_3 \rightleftharpoons HA + HCO'_3$, resulting in an increase in the concentration of bicarbonate ion, and consequently, a decrease in the concentration of hydrogen ion and a decrease in the correction to be deducted from the conductivity of the solution. There is no difficulty in calculating the concentrations of the various ionic and molecular species and so obtaining this correction with ample accuracy; but the method involves the assumption that carbonic acid is the only impurity present in appreciable amounts. The simplest way to test this assumption was to carry out measurements on a single salt in samples of water of appreciable, and widely differing, conductivities. The results for sodium mandelate are given in Table I and in the figure: $\Lambda_1$ is the equivalent conductivity calculated from the "normal" solvent correction, *i.e.*, after subtracting the conductivity of the solvent from that of the solution; $\Lambda_2$ is the equivalent conductivity obtained by applying the combined solvent and hydrolysis correction on the assumption that the conductivity of the solvent is wholly due to carbon dioxide. In the figure, the $\Lambda_1$ values form the lower series of points, the $\Lambda_2$ the upper series, and it is clear that the $\Lambda_2$ values are slightly over-corrected, since the triangulated points of Run 1 have become the highest, instead of being the lowest, values, and the average slope

is slightly greater, instead of being less, than the theoretical Onsager slope. For this reason we think that the continuous line of the figure, which is drawn with the theoretical slope, best represents the true conductivity of sodium mandelate, and we accordingly take $\Lambda_0 = 79{\cdot}35$ as the equivalent conductivity at infinite dilution. We do not think that this is in error by more than 0·10 unit. Assuming a temperature coefficient of 0·024 per degree, $\Lambda_0 = 79{\cdot}51$ at 25°, and taking the mobility of the sodium ion as 50·11 (Robinson and Davies, *loc. cit.*), the mobility of the mandelate ion becomes 29·40 at 25°, or 29·34 at 24·915°. From Shedlovsky's results we obtain $\Lambda_0 = 426{\cdot}27$ for hydrochloric acid, and 76·39 for the mobility of the chloride ion at 25° (Robinson and Davies, *loc. cit.*). Subtraction gives 349·88 for the mobility of the hydrogen ion at 25°, which, with the temperature coefficient 0·015 (Landolt–Börnstein Tabellen, 5te Aufl., p. 1104), becomes 349·43 at 24·915°, and hence for mandelic acid $\Lambda_0 = 378{\cdot}77$. Using this value, we have




calculated $K$, the true dissociation constant of mandelic acid, by means of the Debye–Hückel and Onsager limiting equations. The results are in Table V.

TABLE V.

| $C \times 10^4$. | Λ. | $K \times 10^4$. | $C \times 10^4$. | Λ. | $K \times 10^4$. | $C \times 10^4$. | Λ. | $K \times 10^4$. | $C \times 10^4$. | Λ. | $K \times 10^4$. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1·1149 | 306·69 | 3·844 | 7·3771 | 193·50 | 3·850 | *18·565 | 140·19 | 3·899 | 29·045 | 117·44 | 3·880 |
| 2·2647 | 268·29 | 3·866 | *11·757 | 165·70 | 3·889 | 21·454 | 132·39 | 3·883 | *34·329 | 109·95 | 3·899 |
| 3·6703 | 239·09 | 3·914 | 13·190 | 158·65 | 3·863 | 22·938 | 128·91 | 3·866 | 41·414 | 101·50 | 3·874 |
| *5·7023 | 210·35 | 3·879 | 14·006 | 155·36 | 3·873 | *26·110 | 122·72 | 3·895 | 62·307 | 85·44 | 3·877 |

The degree of dissociation varies between approximately 20 and 80%, a greater range, we believe, than has hitherto been studied for any weak electrolyte, and the mean value of the dissociation constant is $3{\cdot}878 \times 10^{-4}$. The values for the *l*-acid (marked in Table V by asterisks) are consistently high, giving a mean value $K = 3{\cdot}891 \times 10^{-4}$; a possible explanation of this would be the presence of approximately 0·1% of non-conducting impurity in the inactive acid, but as only one run was carried out on the active acid, we take $K = (3{\cdot}88 \pm 0{\cdot}01) \times 10^{-4}$ as the best value for both forms of the acid.

The conductivities of the more concentrated solutions of sodium and barium mandelates were measured for comparison with the extended forms of the Onsager equation previously proposed (Davies, *Trans. Faraday Soc.*, 1927, **23**, 351; Righellato and Davies, *ibid.*, 1930, **26**, 592). In Table IV (*a*), col. 2 shows the measured conductivities for sodium mandelate, and col. 3 gives the values calculated from the extended equation (cf. Robinson and Davies, *loc. cit.*). The good agreement shows that the whole

change of conductivity with concentration is to be attributed to changes in the mobiliti of the ions, and that sodium mandelate is completely dissociated at concentrations up t 0·1N.

The measurements on barium mandelate shown in Table IV (*b*) lead to quite a differen result. The calculated conductivities shown in col. 3 are obtained from the equatio $\Lambda = 92\cdot79 - 162\cdot4\, f_{12}(C)$; here the figure $\Lambda_0 = 92\cdot79$ has been obtained from Shedlovsk and Brown's value, 63·59, for the mobility of the barium ion (*J. Amer. Chem. Soc.*, 1934 **56**, 1066), which, with a temperature coefficient of 0·024 per degree (Landolt–Börnstein *loc. cit.*), becomes 63·45 at 24·915°; 162·4 is the theoretical Onsager slope, and the values of $f_{12}(C)$ are taken from Righellato and Davies's paper. It will be seen that these calculated conductivities are considerably higher than the measured conductivities of col. 2. We have assumed that the discrepancy is due to the presence of the intermediate ion formed by the process: $Ba^{\cdot\cdot} + C_6H_5\cdot CH(OH)\cdot CO'_2 \longrightarrow C_6H_5\cdot CH(OH)\cdot CO_2Ba^{\cdot}$, and have calculated the extent to which this association occurs, assuming the value 30 for the mobility of the intermediate ion and using the method previously described (Righellato and Davies, *loc. cit.*). The results are in Table IV (*b*), where $(1 - \alpha)$ represents the fraction of barium in the form of intermediate ion; an error of 20% in the value assumed for the mobility of the intermediate ion would lead to an error of 5% in $(1 - \alpha)$. Col. 5 of the table shows the dissociation constant, $K = \frac{\{Ba^{\cdot\cdot}\}\{M'\}}{\{BaM^{\cdot}\}} = \frac{F.\alpha(1 + \alpha)m}{1 - \alpha}$, where M represents the mandelate radical, $m$ is the molar concentration, and $F$ is an activity factor. $F$ was calculated from the Brönsted extension of the Debye–Hückel equation, $-\log F = 2\sqrt{I} - BI$, in which $I$ is the ionic strength, given by $I = (1 + 2\alpha)m$, and $B$ is an adjustable constant which was assigned the value 2·83. The values found for $K$ are extremely constant, but as only three measurements were made, we regard the constant $K = 0\cdot17$ as provisional, and intend to check it by an independent method. With it may be compared the values for barium salts previously determined: chloride, $> 1$; nitrate, 0·12; chlorate, 0·20; bromate, 0·14; iodate, 0·08.

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BATTERSEA POLYTECHNIC, LONDON, S.W. 11. [*Received, December 2nd*, 1937.]

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## 19. *Prototropy in Relation to the Exchange of Hydrogen Isotopes. Part III. Comparison of the Rates of Racemisation and of Hydrogen Exchange in a ψ-Acidic Ketone.*

By SHING K. HSÜ, CHRISTOPHER K. INGOLD, and CHRISTOPHER L. WILSON.

According to the ionisation theory of prototropy the rates of enolisation of ψ-acidic ketones should equal their rates of ionisation. Two methods of measuring the rates of enolisation of ketones have been used in the past, *viz.*, by observations on bromination and on racemisation, and it has been shown that both methods give the same result. The rate of ionisation can be measured by observing the rate of hydrogen exchange with a readily ionising solvent. In order to make the observation quantitatively unambiguous it is convenient that the whole of the ionising hydrogen of the solvent should be deuterium. For satisfactory comparison with the former types of measurement it is therefore necessary to repeat either the bromination or the racemisation experiments in the deuterium solvent, inasmuch as the rates of reactions are appreciably affected by the isotopic nature of the solvent independently of whether or not the solvent is a reactant. The rates of racemisation and of deuterium uptake of *l*-phenyl β-*n*-butyl ketone in deuterium oxide–dioxan, with catalysis by deuteroxide ions, have been measured and found equivalent. It is concluded that bromination, racemisation and hydrogen exchange are all controlled by the same fundamental process, which is the ionisation of the ketone.

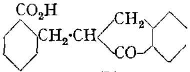
ACCORDING to the ionisation theory of prototropy, $\psi$-acids, such as enolisable ketones and primary and secondary nitro-compounds, constitute a particularly simple set of cases for the quantitative study of mechanism. The special simplicity arises from the circumstance that equilibrium between a $\psi$-acid and its ions is established relatively slowly, whereas the same ions come into equilibrium with the true acid, *e.g.*, the enol or *aci*nitro-compound, practically instantaneously.

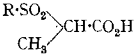
$$\psi\text{-Acid} \underset{\text{slow}}{\rightleftharpoons} \text{Ions} \underset{\text{fast}}{\rightleftharpoons} \text{True acid}$$

This means that, if a pair of ions, formed from the $\psi$-acid, reunite, they nearly always form the true acid and very seldom regenerate the $\psi$-acid. Thus, whereas in prototropy generally the rate of ionisation of one individual is greater by some unknown factor than the rate of its conversion into its isomeride, in the particular case of $\psi$-acidic systems the rate of ionisation of the $\psi$-form may be set equal to the rate of its isomerisation.

It is universally accepted that a large class of hydrogen exchanges, typified, for instance, by the exchange between acetone and water, are dependent on hydrogen ionisation, and hence the opportunity is furnished for a further test of the ionisation theory of prototropy: the test consists in comparing the rate of hydrogen exchange with the rate of isomerisation, where, as in a $\psi$-acid, the rate of isomerisation should equal the rate of ionisation. For instance, we can measure the rate of enolisation of acetone through the rate of its uptake of halogen in aqueous solvents, and, if the ionisation theory is right, this rate should be the rate of ionisation. The rate of hydrogen exchange between acetone and water will certainly measure the rate of ionisation of the acetone, not that of the water which is almost instantaneously ionised. Hence these two rates should be identical for given conditions of temperatures, solvent and catalysis. No test of this character appears as yet to have been made.

We already know of two methods of measuring the rate of enolisation of a $\psi$-acidic ketone, and it is established that they agree. The first is the bromination method, due essentially to Lapworth. The second is applicable when the ketone is optically active and the enol necessarily inactive, for we can then study the change by measurement of the rate of racemisation. The agreement between these two methods was first shown (Ingold and Wilson, J., 1934, 773; Hsü and Wilson, J., 1936, 623) in the example of the ketone (I), and has been confirmed for the carboxylic acids (II) (Ramberg, Mellander, and Hedlund, *Arkiv Kemi, Min. Geol.*, 1934, **11**, B, Nos. 31, 41; 1936, **12**, A, No. 1), and for the ketone (III) (Bartlett and Stauffer, *J. Amer. Chem. Soc.*, 1935, **57**, 2580).


(I.)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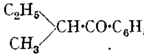
(III.)

In contemplating the comparison of the enolisation rate, measured in either of these ways, with the rate at which the mobile hydrogen undergoes ionic interchange with isotopically labelled, ionisable hydrogen of the medium, we are confronted by an initial difficulty owing to the circumstance that for effective comparison the solvent must be the same: it is not enough that the solvents are isotopic modifications of the same compound, for it is known that the rates of reactions generally, even those which are not dependent on hydrogen exchange, are considerably altered by the substitution of deuterium for protium in the solvent. The above-mentioned bromination and racemisation experiments have, of course, been carried out in ordinary "light" solvents. If we attempt to maintain a substantial identity of solvent by employing for the proposed hydrogen exchange experiments a medium containing only a few units % of its hydrogen in the form of deuterium, we introduce another difficulty, since it has been established that, in one and the same reaction, protons and deuterons are transferred at different specific rates and we do not at the outset know the ratio of these rates. We want to deduce from the experiment the rate at which *original* protons are removed from the ketone; but if, in a mixed protium–deuterium solvent, the places vacated by these protons are

going to be filled by protons and deuterons in a ratio bearing no known relation to the isotopic composition of the solvent, we are no further forward. The simplest way round this difficulty is to employ, in conjunction with the ordinary "light" ketone, a large excess of a protium-free deuterium solvent, so that *every* proton removed from the ketone has its place taken by a deuteron; then a determination of the deuterium uptake will accurately measure the extent of the separation of original protons. But, when comparison is made with the former experiments, the scheme outlined involves a change of solvent, the effect of which on the speed of reaction cannot be disregarded. Therefore the only way of making the comparison satisfactory is to commence by repeating one of the former experiments, a bromination or a racemisation, in a protium-free deuterium solvent, and then to use the same solvent for the measurement of hydrogen exchange.

This has been done with the ketone (III), which was chosen in preference to any acidic substance in order to avoid the complication of an exchangeable carboxylic hydrogen atom. Basic catalysis was employed in preference to acid catalysis, because of the greater theoretical simplicity of the former. We had intended to establish our reference rate in duplicate by measuring both the bromination and the racemisation rates in the pure deuterium solvent, but it turned out that rates convenient for measurement were attained only with more strongly basic catalysts than can be used in association with halogens; our reference rate is therefore based on measurements of racemisation. The solvent, both for these measurements and for those on hydrogen exchange, was a mixture of dioxan and deuterium oxide (about 2 : 1). The catalyst was sodium deuteroxide (about 0·13N), and the temperature 35·0°. The reaction was allowed to run for various known times in the thermostat, and was then stopped by large dilution with water, a process shown to cause no error; the isolated ketone was first polarimetrically examined and then burnt. The density of the combustion water gave, of course, the deuterium content of the whole of the hydrogen of the compound, and this value had to be multiplied by 14 in order to obtain the proportion of deuterium in the single position in which the hydrogen is exchangeable. Both sets of results, which conform to the first-order rate law, are included in the following table.

*Comparison of the Rates of Racemisation and Hydrogen Exchange of* l-*Phenyl* β-n-*Butyl Ketone in Deuterium Oxide–Dioxan containing Sodium Deuteroxide.*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Time (hours) | | 0·00 | 1·00 | 2·00 | 3·25 | 4·00 | 6·50 |
| Racemisation | $\alpha_D$ ($l$ = 10 cm.) | −4·43° | −3·92° | −3·12° | −2·62° | −2·38° | −1·54° |
| | Activity loss (%) [*R*] | 0·0 | 11·6 | 27·3 | 40·9 | 46·2 | 65·2 |
| Hydrogen exchange | Combn. $H_2O$ : Δ*d* (p.p.m.) | — | 774 | 1887 | 2952 | 3152 | 4380 |
| | Combn. $H_2O$ : D (atoms %) * | — | 0·72 | 1·76 | 2·75 | 2·94 | 4·08 |
| | Labile atom : D (atoms %) [*E*] | — | 10·1 | 24·6 | 38·5 | 41·2 | 57·1 |
| Activity loss/D uptake [*i.e.*, *R*/*E*] | | — | 1·15 | 1·11 | 1·06 | 1·12 | 1·14 |

* The figures in the corresponding line in the table of a former paper (Ingold, de Salas, and Wilson, J., 1936, 1334) are wrong by a constant factor (to correct, divide by $1{\cdot}08^2$). This makes no material difference, as it was not these derived figures but the observed densities (also tabulated) that were used in the calculations given.

As the last line of the table shows, racemisation proceeds rather uniformly about 12% faster than corresponds to the apparent rate of hydrogen exchange. This small difference can be explained as follows. The material which has hitherto been called pure deuterium oxide was not, in fact, quite pure. We at first believed the specimen used to contain 99·95 atoms % of deuterium, but, when it was too late to retract, an actual measurement of density showed the deuterium content to be only 99·16 atoms %. Furthermore, owing to the liberation of protons from the ketone during the experiments, the deuterium content, averaged through a run, of the aqueous part of the solvent was still lower, ranging in the different runs between 98·9% and 99·1%; thus for the whole series it is true to say that approximately 1% of the available hydrogen of the medium consisted of protium. Now all who have observed the relative rates at which protons and deuterons are transferred in various reactions agree that protons are transferred considerably more rapidly than deuterons: estimates of the ratio of the rates in different cases vary from 3 to "more than 10" (Wynne-Jones, *J. Chem. Physics*, 1934, **2**, 381).

If we make the reasonable assumption that in our case the ratio is 12, this would exactly account for the residual discrepancy; for, while the 99% of deuterium in the available solvent hydrogen were occupying 99, the 1% of protium would occupy not 1 but 12, out of every 99 + 12 vacant places in the ketone; so that the rate of loss of protons from initial combination with carbon would be 111/99 times the rate of deuteron uptake, *i.e.*, it would be 12% greater. In the circumstances we think that the correct conclusion to draw from the experiments is that the rates compared are equal to within the error of experiment.

We may summarise the conclusions reached as a result of this and the previous work on the rates of the reactions of enolisable ketones by means of the following scheme:

| | | |
|---|---|---|
| Bromination in | "light" solvent | proved equal |
| Racemisation in | "light" solvent | |
| | "heavy" solvent | proved equal |
| Hydrogen exchange in | "heavy" solvent | |

It seems clear from these results that all these reactions are controlled by the same fundamental process, and there is no cause to doubt that this is the ionisation of the ketone.

## Experimental.

l-*Phenyl* β-n-*Butyl Ketone*.—*dl*-β-*n*-Butyl alcohol was successively converted by known methods into the chloride and carboxylic acid, the second step being modified by the employment of solid carbon dioxide instead of the gas in the Grignard reaction. Resolution of the acid through the brucine salt by Schütz and Marckwald's method (*Ber.*, 1896, **29**, 52) gave, after one crystallisation of the salt, 55·9% of the acid with $\alpha_D(l = 10$ cm.$) - 2{\cdot}40°$, whilst the salt from the mother-liquor yielded 38·4% of acid with $\alpha_D(l = 10$ cm.$) + 3{\cdot}50°$. The *l*-acid was converted (Bartlett and Stauffer, *loc. cit.*) successively into its chloride and the phenyl ketone, which had b. p. 64°/0·02 mm., $\alpha_D(l = 10$ cm.$) - 4{\cdot}43°$ (Found: C, 82·3; H, 8·58. Calc.: C, 81·5; H, 8·64%).

*Racemisation and Hydrogen Exchange*.—Equal portions of the *l*-ketone (1·463 g.), delivered from a pipette, were heated severally in sealed bulbs for known times at 35·00° ± 0·01° with mixtures of well-dried dioxan (20·0 c.c.) and 99·16% deuterium oxide (9·0 g.), in which sodium (0·0861 g.) had previously been dissolved, the weight of sodium being standardised by passing wire through a length of capillary tubing and cutting off the projecting ends. The rest of the technique has been outlined in the introduction or in previous papers, the method of combustion being that described by Wilson (J., 1936, 1552; cf. also J., 1934, 493, 1593; 1935, 492; 1936, 1328, 1550). The pyknometer employed was a little smaller than usual, *viz.*, 0·6 c.c. The accuracy of the density measurements was ± 2 p.p.m., and of the polarimetric readings ± 0·01°.

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# 20. *Isotopic Exchange Reactions of Organic Compounds. Part II. A Survey of the Monocarboxylic Acid Series.*

By D. J. G. Ives.

The present work is concerned with the isotopic exchange reactions of hydrogen linked with carbon in a series of monocarboxylic acids. The existing evidence on the exchange reaction of acetic acid is conflicting, but it is now shown that exchange of the methyl hydrogen occurs in alkaline aqueous solution, but not in neutral solution, as previously reported.

It has also been found that phenylacetic, acrylic, crotonic, and sorbic acids undergo alkali-catalysed exchange reactions, whereas propionic, butyric, *iso*butyric, benzoic,

*p*-toluic, α- and β-phenylpropionic, and cinnamic acids do not. No exchange accompanies the acid hydrolysis or saponification of ethyl acetate. These results are discussed in relation to the mechanism of exchange reactions with reference to evidence available from chemical reactions and to theories of structure.

A modified and improved density method of isotopic analysis, accurate to a few parts per million and suitable for small samples, is described.

THE use of deuterium as an indicator in the hydrogen exchange reactions of organic compounds has provided a method of studying not only acidic, pseudo-acidic, and tautomeric substances, but also other compounds which are not normally included in these categories. The method is of unique value because it can provide information in connexion with theories of structure under reversible conditions and is capable of reaching hydrogen atoms linked directly with carbon. It depends neither on the behaviour of molecules under more or less drastic and irreversible reaction conditions, where considerable energy changes may occur, nor on the behaviour of specialised groups in the molecules, and is therefore correspondingly more general in application.

The present work is concerned with the exchange reactions of monocarboxylic acids under conditions in which exchange of the carboxylic hydrogen and exchange proceeding by substitution (Ingold, Raisin, and Wilson, J., 1936, 1637, 1643) are both excluded.

In Part I (Ives and Rydon, J., 1935, 1735) no exchange was detected in the case of butyric acid, a result which was unexpected from some aspects; results which have been recorded for acetic acid are somewhat conflicting, but Liotta and La Mer (*J. Amer. Chem. Soc.*, 1937, **59**, 946) summarise the earlier evidence and indicate that any exchange reaction which may occur must be extremely slow. Acetic, propionic, butyric, and *iso*butyric acids were therefore chosen for the first section of this work, with the object of deciding whether exchange occurs or not in the saturated aliphatic acids. The scope of the work has been restricted by the fact that the exchange reactions which were observed were catalysed by alkali, but proceeded at a rate not much greater than the attack of the alkali on the glass reaction vessels. This circumstance precluded measurements of reaction velocities because the catalyst was progressively destroyed during the course of the reaction. A comparison of the behaviour of different acids has therefore been made under standardised conditions and has not only provided results of some interest, but has also indicated those systems which will repay further study with suitably modified technique.

The method, fully described in the experimental section, was contrived to avoid loss or fractionation at any stage. In the majority of cases the acids were treated with 5 mols. % excess of sodium hydroxide in N-solution at 100°. After neutralisation of the catalyst, both solvent and solute were analysed isotopically by a semi-micro density method. It is believed that this method of studying exchange reactions is adequate for definite qualitative conclusions and for providing an indication of the relative magnitudes of well separated velocities. The results for the saturated acids are shown in Table I, in which cols. 4 and 5 give the actual analytical figures for the mol.-fractions of deuterium oxide in the solvent and in the water produced by combustion of the solute respectively. The former do not represent the true isotopic compositions of the solvents during the actual exchange reactions because of the water of neutralisation which is subsequently added. This has been taken into account in calculating the exchange numbers shown in col. 6; these are the apparent numbers of hydrogen atoms exchanged on the assumption that there is no isotopic discrimination during the exchange reaction (cf. Small and Wolfenden, J., 1936, 1811).

The experiments in neutral and acid solutions were included for purposes of comparison with the results of Hall, Bowden, and Jones (*J. Amer. Chem. Soc.*, 1934, **56**, 750), Wynne-Jones (*Chem. Reviews*, 1935, **17**, 115), and Erlenmeyer, Schoenauer, and Schwartzenbach (*Helv. Chim. Acta*, 1937, **20**, 726), who find exchange with the acetate ion in neutral solution, and of Klar (*Z. physikal. Chem.*, 1934, *B*, **26**, 335), who reports an acid-catalysed exchange reaction with acetone. It is clear that, although acetic acid shows a very slow exchange reaction in an alkaline medium, the other acids show none (see next paragraph), and in neither of the cases studied does exchange occur in neutral or acid media. Whilst an

TABLE I.

| Acid. | Conditions. | Time, hrs. | Mol.-fraction $D_2O \times 10^5$. Solvent. | Solute. | Exchange number. |
|---|---|---|---|---|---|
| Acetic | 5 Mols. % excess NaOH | 100 | 2442 | 135 | 0·161 |
| ,, | ,, ,, ,, | 200 | 2265 | 232 | 0·300 |
| ,, | ,, ,, ,, | 400 | 2263 | 315 | 0·407 |
| ,, | Neutral | 100 | 2460 | 8 | — |
| ,, | 5 Mols. % excess $H_2SO_4$ | 100 | 2433 | 8 | — |
| Propionic | ,, ,, NaOH | 400 | 2271 | 18 | 0·039 |
| Butyric | ,, ,, ,, | 405 | 2244 | 6 | 0·017 |
| ,, | 20 ,, ,, ,, | 405 | 2410 | 45 | — |
| ,, | Neutral | 100 | 2460 | 2 | — |
| ,, | 5 Mols. % excess $H_2SO_4$ | 100 | 2433 | 5 | — |
| *iso*Butyric | ,, ,, NaOH | 400 | 2268 | 5 | 0·015 |
| | *Experiments with ethyl acetate.* | | | | |
| Saponification | | 24 | *ca.* 2000 | 15 | — |
| Acid hydrolysis | | 24 | *ca.* 2000 | 2 | — |

apparent exchange reaction may conceivably be due to experimental error (particularly when the changes in the density of the solvent alone are measured), this can hardly be so when a negative result is obtained. The previous data on the exchange of the acetate ion in neutral solution must therefore be revised, with the possible exception of the observation by Goldfinger and Lasareff (*Compt. rend.*, 1935, **200**, 1671) that exchange occurs on standing for 11 months.

In all cases there is a very small apparent exchange, but a slight deviation from exact stoicheiometric equivalence, in either direction, during the final neutralisation of the catalyst is sufficient to account for an error of these dimensions. The result with propionic acid is very close to this margin of error and cannot be taken as real evidence of exchange. Butyric acid in presence of 20 mols. % excess of sodium hydroxide shows an appreciable exchange effect, bnt in this case the attack of the alkali on the glass reaction vessel was very extensive and the major part of the apparent exchange can be accounted for by the presence of $Na_2SiO_3,H_2O$, which cannot readily be dehydrated at 100°, in the dried solute.

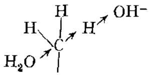
It is highly probable that the mechanism of the acetic acid exchange reaction is identical with that of three-carbon prototropy activated by the carboxyl group in so-called pentad keto-enol tautomerism (Ingold, Shoppee, and Thorpe, J., 1926, 1477). Enolisation in acetic and other monocarboxylic acids or esters has frequently been postulated to explain various modes of reaction (see Part I) and has been extensively discussed in relation to racemisation (McKenzie and Wren, J., 1919, **115**, 602; Conant and Carlson, *J. Amer. Chem. Soc.*, 1932, **54**, 4048; Wilson, J., 1934, 98), but on the other hand, the existence of acetic acid in an enolic form has been rejected (Watson, J., 1925, 2067; *Chem. Reviews*, 1930, **7**, 173). Enolisation is usually interpreted as the formation of an enol, or enolate ion, either as a stable entity or, at least, as a transitory reaction phase with real free existence. Ingold (J., 1933, 1120), however, has rejected the view that the anion of a prototropic system has the enol form, and has suggested that it is, in fact, mesomeric. If this is so, it is clear that prototropy, even when acid-catalysed, does not necessarily involve enolisation (cf. Ingold and Wilson, J., 1934, **93**, 773). Enolisation may in many cases accompany prototropy, because the rate of transformation of the mesomeric ion into the enol form is generally more rapid than its rate of transformation into the keto-form (Hsü and Wilson, J., 1936, 623; but not always, cf. Kimball, *J. Amer. Chem. Soc.*, 1936, **58**, 1963), but this is rather a side reaction than the primary cause of the hydrogen lability.

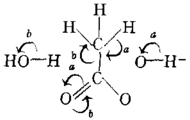
Since the carbonyl group in its normal state is a hybrid of the non-polar with the semipolar form (Baker and Ingold, J., 1927, 832; Pauling and Sherman, *J. Chem. Physics*, 1933, **1**, 606; McKay, *Chem. and Ind.*, 1934, **53**, 870), it may be suggested that this degeneracy extends to other parts of the molecule, and that the exchange reaction of acetic acid, or acetone, is primarily a function of the normal configuration of the molecule, rather than of any specific act of enolisation. It is, of course, probable that at the moment of attack electromeric adjustment occurs within the molecule along the path laid down by the mesomeric system. The exchange reaction of acetone has been tentatively ascribed to

enolisation (Schwartz and Steiner, *Z. physikal. Chem.*, 1934, *B*, **25**, 153; Halford, Anderson, and Bates, *J. Amer. Chem. Soc.*, 1934, **56**, 491) and quite definitely by Urey and Teal (*J. Mod. Physics*, 1935, **7**, 34), but it has been admitted that enolisation is not necessarily involved (Halford, Anderson, Bates, and Swisher, *J. Amer. Chem. Soc.*, 1935, **57**, 1663). If the circumstance be considered that both enolisation by the basic mechanism and base-catalysed exchange must be conditioned by the removal of an α-hydrogen atom (Watson and Yates, J., 1932, 1207), whether this is the initial step or not (cf., *inter alia*, Watson, Nathan, and Laurie, *J. Chem. Physics*, 1935, **3**, 170), it is clear that these must be parallel reactions, and cannot, therefore, be related as cause and effect.

The exchange reaction of acetic acid may, perhaps, be related to the "methyl effect" of Baker and Nathan (J., 1935, 1844), and it is of interest that Baker, Nathan, and Shoppee (J., 1935, 1847) conclude that this effect is mesomeric in type. This is supported by the observation of Pauling and Sherman (*loc. cit.*) that the C=O bond energy is considerably changed as hydrogen attached to carbon is replaced by alkyl, this change being attributed to the interaction with the carbonyl group of other bonds in the molecule. Further, the large difference between the dissociation constant of formic acid ($1{\cdot}87 \times 10^{-4}$; recalculated from the data of Auerbach and Zeglin, *Z. physikal. Chem.*, 1922, **103**, 191) and acetic acid ($1{\cdot}753 \times 10^{-5}$; MacInnes and Shedlovsky, *J. Amer. Chem. Soc.*, 1932, **54**, 1429) may possibly be attributed, not only to the admittedly small inductive effect of the methyl group, but also to a "conjugational effect," similar to that which reduces the strength of αβ-unsaturated acids (Ives, Linstead, and Riley, J., 1933, 561).

The mechanism of the exchange, however, cannot be regarded as definitely established. One possibility only can be excluded: the exchange reaction of chloroform (Horiuti and Sakamoto, *Bull. Chem. Soc. Japan*, 1936, **11**, 627) is probably activated by an inductive effect ($-I$), but this cannot be so in the case of the exchange reaction of acetic acid in alkaline solution, since the species concerned are acetate ions, in which the free negative pole would provide a powerful $+I$ effect (Waters, "Physical Aspects of Organic Chemistry," p. 214), in a sense to retard an exchange reaction. Exchange by an inductomeric effect (Ingold, *Chem. Reviews*, 1934, **15**, 225), which would be facilitated in an anion as compared with a neutral molecule, cannot be definitely rejected. A further question relates to whether the reaction is bimolecular or termolecular (Hsü, Ingold, and Wilson, J., 1935, 1778): its slowness might suggest the latter, but since the points of removal and addition of the proton are coincident, this would probably involve a Walden inversion of the type (I).

(I.) 


 (II.)


It is, however, possible to visualise a tautomeric termolecular mechanism in which the intermediate stage would not attain kinetic independence; this is illustrated in the scheme (II), in which processes (*a*) and (*b*) occur as one continuous operation, wherein the system is never separated into its component ions and molecules until the exchange reaction is completed.

The absence of exchange with propionic, butyric, and *iso*butyric acids, as compared with acetic acid, is in accordance with the known inductive effect ($+I$) of alkyl groups (methyl, ethyl, and two methyl groups respectively) which tend to charge the α-carbon atom negatively and retard exchange: as would be expected, this effect is in the opposite direction to that observed in exchange reactions promoted by an electrophilic catalyst (Ingold, Raisin, and Wilson, J., 1936, 1643). It has also been observed in other connexions that the hydrogen in the α-position to carbonyl is least reactive to a protophilic reagent when it is tertiary and most active when it is primary, whereas the reverse is true with respect to an electrophilic reagent (cf. Bartlett and Stauffer, *J. Amer. Chem. Soc.*, 1935, **57**, 2580). On the views expressed above, exchange of hydrogen elsewhere than in the α-position is not to be expected in saturated acids.

Lowry's mechanism of hydrolysis of esters (J., 1925, **127**, 1379) involves the development of the carbonyl group into its fully activated form, which might be supposed to promote an exchange reaction in the α-position. It has also been shown that certain optically active esters are more readily racemised by alkali than are the parent acids (Gadamer, *J. pr. Chem.*, 1913, **87**, 312; Wren, J., 1918, **113**, 210). For this reason, both acid and alkaline hydrolyses of ethyl acetate were carried out in a " heavy " medium, the technique being similar to that employed with the acids. The difficulty of manipulation was greater, and the results shown in the last two lines of Table I, were negative: the slight effect observed in the case of saponification is probably within experimental error.

The remainder of the work now recorded deals with the influence of aryl substitution and unsaturation on the primary exchange reaction of acetic acid. The results are collected in Table II. The conditions were the same in each case: 5 mols. % excess of sodium hydroxide in N-solution; 100 hrs.; 100°.

TABLE II.

| Acid. | Mol.-fraction of $D_2O \times 10^5$. Solvent. | Solute. | Exchange number. | Acid. | Mol.-fraction of $D_2O \times 10^5$. Solvent. | Solute. | Exchange number. |
|---|---|---|---|---|---|---|---|
| Phenylacetic ......... | 2229 | 575 | 1·765 | β-Phenylpropionic... | 2220 | 8 | 0·032 |
| ,, ......... | 2185 | 568 | 1·779 | α- ,, ... | 2220 | 16 | 0·063 |
| Benzoic .............. | 2224 | 2 | 0·004 | Acrylic .............. | 2214 | 276 | 0·365 |
| *p*-Toluic .............. | 2224 | 2 | 0·006 | Crotonic .............. | 2265 | 270 | 0·582 |
| Cinnamic .............. | 2265 | 5 | 0·015 | Sorbic .................. | 2215 | 160 | 0·493 |

The error in the exchange number is directly proportional to the total number of hydrogen atoms per molecule of the acid; the agreement between the duplicate phenylacetic acid experiments therefore indicates an adequate degree of accuracy for the present purposes.

The most striking result, on first inspection, is the apparently anomalous effect of substitution in the two series starting with acetic and acrylic acids. In the former, phenyl substitution promotes exchange (acetic, $E = 0{\cdot}161$; phenylacetic, $E = 1{\cdot}77$) and methyl substitution stops it (propionic, $E = ca.\ 0{\cdot}004$); in the latter, the reverse is true (acrylic, $E = 0{\cdot}365$; cinnamic, $E = 0{\cdot}015$; crotonic, $E = 0{\cdot}568$). It is believed that this anomaly is satisfactorily explained in the following discussion of the separate cases.

*Phenylacetic Acid.*—The tautomeric effect of the phenyl group ($\pm T$) provides an additional means of release of the δ — charge induced on the α-carbon atom by the attack of the hydroxyl ion at the α-hydrogen atoms: an increased rate of exchange, as compared with acetic acid, is therefore only to be expected. That the activating effect of the phenyl group in this respect is less than that of the carboxyl group is shown by comparison with malonic acid, of which the methylene hydrogen exchanges readily in neutral solution (Münzberg, *Z. physikal. Chem.*, 1935, *B*, **31**, 18; Halford and Anderson, *J. Amer. Chem. Soc.*, **1936**, **58**, **736**), and conforms with the inferior efficiency of the phenyl group in activating three-carbon tautomerism (Ingold and Piggott, J., 1922, **121**, 2381). The exchange reaction also corresponds with the known activity of the methylene hydrogen in phenylacetic acid (Perkin condensation; Pschorr, *Ber.*, 1896, **29**, **496**), but since it is the first example of definite prototropy in a saturated compound containing a phenyl group and a single carboxyl group, it is of interest in connexion with the fact observed by McKenzie and Wren (J., 1920, **117**, 680) that α-aryl-substitution is a necessary condition for the racemisation by alkali of carboxylic acids in which the α-carbon atom is the centre of asymmetry and carries a hydrogen atom (cf. Wilson, *loc. cit.*).

*Benzoic,* p-*Toluic, and* β-*Phenylpropionic Acids.*—The absence of exchange in these cases was not unexpected and is in accord with generally accepted electronic theory. It is probable that the methyl hydrogen of *p*-toluic acid would exchange under the influence of a more active catalyst (cf. Kharasch, Brown, and McNab, *J. Org. Chem.*, **1937**, **2**, **36**, who find exchange with *p*-nitrotoluene catalysed by sodium ethoxide). A comparison of *p*-toluic and phenylacetic acids on the one hand with vinylacetic and crotonic acids (Part I, *loc. cit.*) on the other, indicates that the ethylenic bond is more polarisable than the phenyl

group, both in the activation of exchange and in the transmission of electromeric effects (cf. Waters, J., 1933, 1551).

*α-Phenylpropionic Acid.*—The absence of exchange in this case was unexpected. On polar grounds, it seemed unlikely that the feeble inductive effect of the methyl group could entirely counterbalance the activating tautomeric effect of the phenyl group, and an exchange reaction slower than that of phenylacetic acid, but still appreciable, was anticipated. The influence of steric hindrance, however cannot be excluded, since the exchange reaction is similar in type to the anion substitutions discussed by Ogg and Polanyi (*Trans. Faraday Soc.*, 1935, **31**, 604) in which steric effects play a major part. It is also noteworthy in this connexion that α-alkyl hindrance is very appreciable in the saponification of esters (Bryant and Smith, *J. Amer. Chem. Soc.*, 1936, **58**, 1014).

*Acrylic Acid.*—The slow exchange reaction in this case was not unexpected, since a $\delta +$ charge on the β-carbon atom has been postulated in connexion with the Michael reaction (Cooper, Ingold, and Ingold, J., 1926, 1868) and with hydrogen halide addition (Lucas and Jameson, *J. Amer. Chem. Soc.*, 1924, **46**, 2475); this may be supposed to facilitate the removal of a β-hydrogen atom as a proton. It may also, perhaps, be inferred from the high polarisability of the ethylenic link that the β-hydrogen atoms in acrylic acid would resemble the methyl hydrogens of acetic acid in reactivity. The mechanism of this particular exchange is discussed in relation to that of crotonic acid.

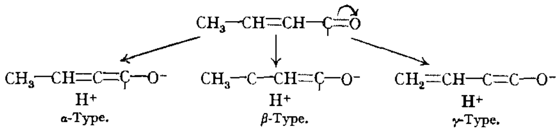
*Crotonic Acid.*—The apparently anomalous effect of the methyl group in promoting exchange disappears if the methyl hydrogen itself is concerned in the exchange reaction, which, *ipso facto*, constitutes evidence that such is the case. This is further supported by the reactivity of the methyl group in crotonic acid in the Claisen reaction with oxalic ester (Lapworth, J., 1901, **79**, 1276). The question of whether the methine hydrogen is also involved is of some importance, and will provide the subject of a further communication.

It might be suggested that the exchange reaction of crotonic acid is due to an equilibrium with its isomeride vinylacetic acid. Such an equilibrium, however, must be preceded by an ionisation of the γ-hydrogen, and it is this initial process, rather than any subsequent change, which is the subject of the present discussion. The slowness of the crotonic acid exchange reaction indicates that the position of such an equilibrium, if it exists at all, must be very close to 100% αβ.

*Sorbic Acid.*—This acid is of interest in so far as it contains a conjugated system. Again, the evidence of the Claisen reaction (Borsche and Manteuffel, *Ber.*, 1932, **65**, 868) indicates that the methyl hydrogen is involved, but on the other hand, Waters (J., 1933, 1551) ascribes less polarisability to a conjugated chain than to a phenyl group: on this basis a comparison with *p*-toluic acid would imply no exchange on the part of sorbic acid. The possibility that the hydrogen on alternate carbon atoms (β and δ) may be involved cannot be excluded (Lapworth, J., 1898, **73**, 445; Bloom and Ingold, J., 1931, 2765), and it is therefore clear that, whilst the identity of the exchanging hydrogen remains undefined, certain anomalies in the interpretation of the results of exchange experiments must remain.

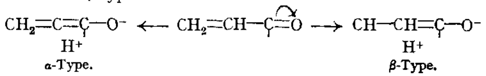
Some evidence, however, may be gathered by considering the possible mechanisms of the exchange reactions with reference to the constitution of the intermediate ions. Crotonic and acrylic acids are discussed for this purpose, since they probably represent two different modes of reaction. It is assumed that the primary electron-release effect which activates exchange is the tendency of the carbonyl group to assume a dipolar form: $>C{=}O \longrightarrow >\overset{+}{C}-\overset{-}{O}$, and that this tendency is transmitted electromerically to the seat of exchange. This is justified in the case of the αβ-unsaturated acids by the evidence of the depression of the dissociation constants of such acids by the so-called "conjugational effect" (Ives, Linstead, and Riley, *loc. cit.*; Dippy and Lewis, J., 1937, 1008), which postulates a path along which electromeric adjustment can occur between the carboxyl group and the rest of the molecule: the dissociation of the acid is concerned with one end of this path, and the exchange reaction with the other.

For the sake of clarity, we shall assume that the intermediate ion has the unperturbed enol form; that the exchange of α-, β-, or γ-hydrogen in crotonic acid must involve quite characteristic and different types of intermediate ion is clear from the following scheme:

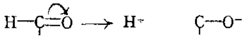



The three possibilities are denoted the α-, β-, and γ-types of exchange, and require the following structural changes to accompany the formation of the ion. (1) α-Type: no valency disturbance; loss of conjugation with development of allene structure. (2) β-Type: the formation of a bivalent carbon atom; loss of double bond and therefore loss of conjugation. (3) γ-Type: no valency disturbance; no loss of conjugation.

Consideration of the probable energy requirements of these operations indicates that terminal exchange is most likely in crotonic acid, and, also, in sorbic acid for similar reasons. Again, this problem is of interest in connexion with the "methyl effect" of Baker and Nathan (*loc. cit.*). On the other hand, the exchange reaction of acrylic acid is necessarily of the α- or β-type:




and the exchange reaction of formic acid (Small and Wolfenden, *loc. cit.*; Münzberg, *loc. cit.*) would appear, paradoxically, to be of the β-type (bivalent carbon, loss of double bond):



*Cinnamic Acid.*—The lack of exchange can be attributed to the direct coupling of the carboxyl double bond with the phenyl group by means of the ethylenic link. This depression of reactivity indicates that the molecule has a mesomeric structure; evidence in support of this view is available from the following sources.

(1) Resonance energies, calculated from the data given by Pauling and Sherman (*loc. cit.*), Pauling (*J. Amer. Chem. Soc.*, 1932, **54**, 3570), Kharasch (*Bur. Stand. J. Res.*, 1929, **2**, 359), and Landolt–Börnstein are recorded, in volt-electrons, in Table III, the possible error in the values amounting to about 0·2 v.-e.

TABLE III.

| | | | | | |
|---|---|---|---|---|---|
| Acetic acid | 1·33 | Acrylic acid | 1·30 | Benzoic acid | 3·26 |
| Propionic acid | 1·37 | Crotonic acid | 1·45 | Phenylacetic acid | 2·80 |
| Butyric acid | 1·29 | Sorbic acid | 1·86 | *p*-Toluic acid | 2·98 |
| *iso*Butyric acid | 1·53 | | | β-Phenylpropionic acid | 2·95 |
| | | | | Cinnamic acid | 3·66 |

| | |
|---|---|
| Phenyl (Pauling and Sherman, *loc. cit.*) | 1·71 |
| " from β-phenylpropionic and propionic acids | 1·58 |
| " from phenylacetic and acetic acids | 1·47 |
| " from cinnamic and acrylic acids | *2·36* |
| —CH=CH— from crotonic and acetic acids | 0·12 |
| " from cinnamic and benzoic acids | *0·40* |
| —CH=CH— replacing $-CH_2-CH_2-$ from crotonic and butyric acids | 0·16 |
| —CH=CH— replacing $-CH_2-CH_2-$ from cinnamic and β-phenylpropionic acids | *0·71* |

Intercomparison of these results in the manner indicated in the table shows that the resonance energy of cinnamic acid is higher than would be anticipated, by about 0·5 v.-e. (12 kg.-cals.), which is considerably greater than any likely error in the thermal data. Other points of interest will be apparent from these figures.

(2) The influence of phenyl substitution in three-carbon tautomeric systems indicates than an increase of stability results from the formation of a cinnamic acid structure (cf. Baker, "Tautomerism," p. 158).

(3) Cinnamic acid is less ionised than acrylic acid in aqueous solution ($K \times 10^5 = 3·65$

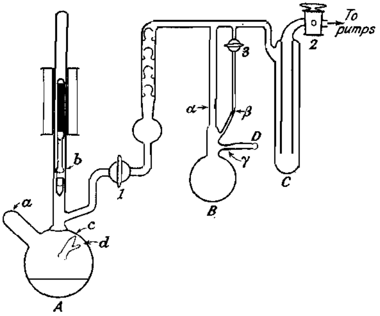
and 5·56 respectively; Dippy and Lewis, *loc. cit.*) : if the strengths of unsaturated acids are mainly conditioned by polarisability (Ives, Linstead, and Riley; cf., however, Dippy and Lewis, *locc. cit.*), the reduced strength of cinnamic acid corresponds with a permanent (mesomeric) polarisation in the molecule.

(4) Finally, Duquesnois (*Bull. Soc. chim.*, 1937, **4**, 193) and Lespagnol and Bruneel (*J. Pharm. Chim.*, 1937, **25**, 454) have shown that cinnamic acid and its aldehyde and esters are less reactive to halogens in the dark than cinnamyl alcohol or styrene. This corresponds with a reduced polarisability of the ethylenic bond (cf. Anantakrishnan and Ingold, J., 1935, 1396) which might be inferred from a mesomeric degeneracy of the molecules containing the conjugated system in question.

## Experimental.

*Preparation of Materials.*—The organic materials were purchased, or prepared by standard methods, and carefully purified. The purity was checked by determination of m. p., b. p., equivalent (by titration), or density. Concentrated carbonate-free sodium hydroxide (prepared from the metal) was rendered 1·050 ± 0·002N. by dilution with 2·5% deuterium oxide and standardised micro-volumetrically. Other standard solutions were prepared similarly. Weighed amounts of 8N-sulphuric acid or anhydrous sodium carbonate were used for neutralisation of the alkaline and acid catalysts respectively.

Fig. 1.




*Exchange Experiments.*—The exchange reactions were carried out in Pyrex bombs of 100 c.c. capacity. These were prepared from Pyrex flasks and were of the form indicated in Fig. 1, where a bomb, *A*, is shown in connexion with the solvent-recovery apparatus. Each bomb carried, in addition to the original neck (*a*), three side tubes; one of these (*b*, 30 mm. × 10 mm.) was closed at the lower end by a septum blown directly into the wall of the flask, and is referred to subsequently as the "fall-tube." The fall-tube was fitted with a closed side branch, near the bomb, by which it could be sealed to the solvent-recovery apparatus when desired. The other two tubes (*c* and *d*) were for the respective purposes of introducing the standard solution and of evacuation immediately before starting the reaction.

The bombs were prepared for use by suitable cleaning and thorough drying in vacuum. Weighed quantities of the standard solutions were introduced, and the bombs left sealed until used. The quantity of the particular acid under investigation, calculated to give a N-solution in the form of the sodium salt, was weighed out into a capsule and introduced through the neck of the bomb (*a*), which had been opened for this purpose. After the neck had been resealed, the contents of the bomb were frozen at a temperature of − 80°, and the bomb rapidly evacuated through the side tube *d*, which was then sealed. After thawing and thorough mixing of the contents, the bomb was placed in a boiling water-bath, or, for the hydrolyses, in a thermostat at 75°.

*Recovery of Water.*—*From solvent.* Before removal of the bomb from the water-bath, at the conclusion of the exchange period, the calculated quantity of the 8N-sulphuric acid was weighed out into a small, stout Pyrex "bucket," which was fitted with a fine platinum hook. This bucket could be suspended from a glass-sheathed armature, for manipulation inside the fall-tube by means of a solenoid. After removal from the water-bath, the bomb was cooled and sealed on to the solvent-recovery apparatus in the position shown in Fig. 1 : the armature, with suspended bucket, was lowered into the fall-tube, and the latter sealed. The apparatus was then cautiously evacuated : any loss by evaporation from the sulphuric acid during this operation represents a negligible error in the subsequent calculations. Tap 1 (Fig. 1) was then closed, a heavy current passed through the solenoid, and the bucket driven through the septum

without allowing the armature to drop. The current through the solenoid was then reduced, the armature raised, and a " shelf " provided on which it could rest by heating the wall of the fall-tube so that it gently " caved in." The contents of the bomb were thoroughly mixed : in some cases, where solid acid separated, prolonged shaking and boiling were necessary before this was complete. Trap *C* was then cooled to $-80°$, tap 1 opened, and the pressure in the apparatus reduced to about 0·01 mm. Tap 2 was then closed, the cooling bath removed from trap *C*, and vessel *B* cooled in ice. The bomb *A* was next surrounded by a water-bath, which was gradually raised to the b. p. and maintained there until the residue in the bomb was dry. Constriction α was then sealed, tap 3 closed, and trap *C* again cooled to $-80°$. The apparatus was then opened to the pumps for a few minutes and subsequently left closed for about ½ hour; any condensate in *C* was now transferred to vessel *B* by suitable manipulation of taps, warming, and cooling. This procedure was repeated until no appreciable condensation of water occurred in trap *C*. The whole of the solvent was then collected in *B* by cooling this to $-80°$ with tap 3 open, and *B* was finally sealed off (at α and β) and removed from the apparatus. After being thawed and mixed, a sample of about 0·3 c.c. of the recovered solvent was poured into the side tube *D* which was provided with a thin-walled end : *D* was then sealed off (at γ) and stored for isotopic analysis.

This whole procedure was applied to all cases, except those in which a neutral medium was used for the exchange reaction : here no neutralisation of the catalyst was required, the bucket was eliminated, and the armature used only as a breaker. In the hydrolysis experiments, the alcoholic solvent was not collected, since a precise knowledge of its isotopic composition was not required. The quantity of sodium carbonate used to neutralise the products of the acid hydrolysis was calculated on the basis of $K = [Me{\cdot}CO_2Et][H_2O]/[EtOH][Me{\cdot}CO_2H] = 4{\cdot}0$.

*From residue.* The bomb was opened, and the dry residue scraped out as completely as possible. After being powdered, it was tested for neutrality with both alcoholic and aqueous phenolphthalein : in the majority of cases it was neutral to the former and slightly alkaline to the latter, in conformity with the required stoicheiometric accuracy, owing to the hydrolysis of sodium salts of weak acids. After transference to a boat, the residue was dried at 100° in a high vacuum, and then burned in dry air or oxygen, the combustion water being collected at $-80°$. Particular care was taken to ensure complete recovery of this water, which was finally transferred in vacuum to a sampling tube similar to that described in connexion with the solvent-recovery apparatus.

*Isotopic Analysis.*—The difficulty of avoiding errors in the density method of isotopic analysis is considerably increased when the quantity of water available is small (in the present case, 0·2—0·4 c.c.); the method described in Part I (*loc. cit.*) has therefore been modified in several important respects, although the general sequence of operations has been retained. Errors due to small losses during purification have been avoided by carrying out the purification, measurement of density, and recovery of the samples in a vacuum; 0·2579 g. of water lost 0·0003 g. in weight after undergoing this sequence of operations three times.

The purification apparatus is illustrated in Fig. 2. All ground joints were lubricated with " Apiezon L " grease. The pumping system consisted of a three-stage mercury-diffusion pump, backed by an oil pump, a trap cooled to $-80°$ to prevent back diffusion of mercury vapour, and a discharge tube as a rough vacuum gauge. Air could be admitted to the apparatus when desired through a suitable purification and drying train. The section of apparatus between the points *a* and *c* was subjected to cleaning operations and final steaming from conductivity water, and the whole apparatus was pumped to a hard vacuum and thoroughly baked before use in each case.

Vessel *A*, which could be opened to the silica combustion tube by the usual device of septum and breaker, was used for the preliminary heating with silver oxide. (The sample was released in *A*, after evacuation, baking, and sealing, by shaking, so that the thin wall of the sample tube was broken.) Trap *B* contained a trace of silver oxide and was cooled to $-80°$ when used as receiver for the distillation of the sample through the combustion tube. During this process, considerable quantities of gas were evolved and it was necessary from time to time to reduce the pressure in the apparatus, but at no stage of the process was continuous pumping necessary. This gas evolution practically ceased (apart from a small residual effect due to the dissociation of the copper oxide) on completion of the distillation. The constriction *a* was then sealed, and the sample kept at room temperature, in presence of the trace of silver oxide, for ½ hour. Trap *C* was now cooled to $-80°$, and the last traces of gas removed from the system by pumping until the ultimate vacuum obtainable was reached. The final distillation into the flotation

vessel $D$ was then carried out, without pumping, with the receiver at $-80°$. On completion of this operation, the flotation vessel was withdrawn by sealing off at the constriction $b$. The avoidance of ebullition during this final distillation was found to be important.

The next stage of the purification was carried out in the flotation vessel, shown in Fig. 3. Bulb $D$, of about 2 c.c. capacity, was used as receiver in the distillation just described, $b$ being the constriction at which the vessel was sealed off from the rest of the apparatus. The sample was poured into the compartment $A$, a thin-ended sampling tube in which the sample was finally recovered. This was followed by a distillation, between 40° and 0°, into the tube $B$, which was of 2 mm. diameter and contained a silica float of volume 10—15 mm.$^3$. The sample was next poured into $D$ through the narrow capillary $C$, rinsed round, and poured back into $A$, with the vessel in an inverted position. This cycle of distillation and pouring operations was repeated 3 or 4 times, with the result that soluble impurities collected in $A$, and the density of the sample decreased to a limiting constant value. The total decrease in density resulting from this procedure was, on the average, about 15 p.p.m., but in some cases was even greater.

FIG. 2.

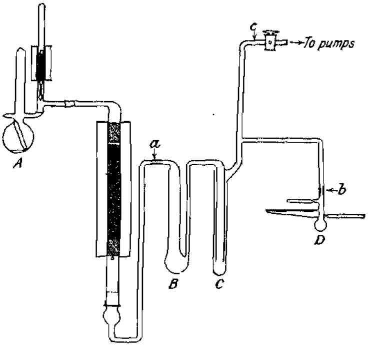
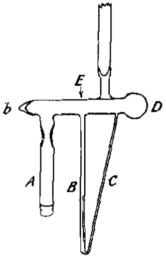



FIG. 3.




A difficulty with " heavy " samples was experienced, owing to the fractionation occurring in the distillation from $A$ into $B$. This was so considerable that the distillate in the narrow tube $B$ was far from homogeneous, being " light " at the bottom and " heavy " at the top (cf. Hall, Anderson, and Jones, *J. Amer. Chem. Soc.*, **1934**, **56**, 749). Diffusion being exceedingly slow, it was necessary to mix the sample by pouring it through $C$ into $D$, rinsing round and pouring it back again, before a measurement could be carried out.

The method of flotation need not be described in detail. The rate of movement of the float was observed and plotted against temperature in the usual way. The difficulty of " sticktion " was avoided by not measuring any rate of motion in excess of about 0·2 mm. per minute, corresponding with a temperature range of about 0·01°. Between each determination the float was removed from the vessel, so that the latter might be steamed, by making an opening at the point $E$. When not in use, the float was kept in fuming nitric acid, and was manipulated by means of a narrow tube with a flat constriction. This provided a holder for the float in which it could be washed, and from which it could be extruded directly into the flotation vessel by means of a thin platinum wire. No difficulty due to fortuitous density changes was experienced with any of the floats used.

The thermostat and thermometer were the same as those used in Part I, but the temperature scale was corrected by calibration against a platinum thermometer with a fundamental interval of 14 ohms. Ice and steam points were determined with the usual precautions and corrections, and the third fixed point necessary to relate platinum and Centigrade temperatures was obtained with the aid of sodium sulphate decahydrate recrystallised to constant transition temperature. The accuracy of the scale thus obtained did not exceed $\pm$ 0·01°, and, in the author's opinion, greater accuracy is unobtainable without great experimental elaboration, particularly with

regard to the fixed points. A check on this scale was provided by the temperature of the transition $MnCl_2,4H_2O \rightleftharpoons MnCl_2,2H_2O$ + satd. soln.: a value of 58·12° was obtained (Richards and Wrede, *Proc. Amer. Acad. Sci.*, 1907, **43**, 343 give 58·09°). The accuracy within the temperature range used (22—32°) was undoubtedly better than indicated by this comparison. Duplicate measurements of the density of "heavy" samples with floats of slightly different density gave substantially identical results, the largest discrepancy observed being 3 p.p.m.

*Calculation of Densities and Mol.-fractions of Deuterium Oxide.*—Tronstad, Nordhagen, and Brun (*Nature*, 1935, **136**, 515) have shown that the earlier values for the specific gravity of deuterium oxide were too high, owing to the presence of $^{18}O$. The earlier data of Lewis and Macdonald (*J. Amer. Chem. Soc.*, 1933, **55**, 3057) and of Luten (*Physical Rev.*, 1934, **45**, 161), however, provide the only information available with regard to the variation of specific gravity with temperature and with mol.-fraction in mixtures with normal water. The earlier figures have therefore been used, and it is clear that any possible error in the exchange numbers from this source must be negligible.

The formula for the density of mixtures of deuterium oxide and normal water was quoted wrongly in Part I (p. 1742): the correct formula is $d_{4^\circ}^{25^\circ} = 0{\cdot}9970 + 0{\cdot}1078x - 0{\cdot}0012x(1 - x)$.

In calculating mol.-fractions of deuterium oxide in the solvent actually used in an exchange reaction, allowance was made for the dilution which occurs on neutralisation of the catalyst. The solvent was examined in every case, but it was not possible to prepare "deuterium balance sheets" because slight variations occurred from experiment to experiment due to small losses, and also possibly small dilutions, in the operations of sealing and exhausting the bombs. The subseqnent procedure, however, must have been so nearly quantitative as to render this precaution superfluous, and in any case, the effect of exchange on the density of the solvent was usually close to experimental error. Such small variations in the solvent do not affect the final result to any appreciable extent, because the solvent remaining *after* these operations was examined in each case.

Densities of normal water at various temperatures were interpolated graphically from the data given in International Critical Tables. Allowance was made for the thermal expansion of the silica float, which has an appreciable effect over the wider temperature range.

The author records his thanks to Dr. H. R. Nettleton for the loan of apparatus and helpfnl advice in connexion with the platinum-resistance thermometry.

Birkbeck College, London, E.C. 4. [*Received, October 20th*, 1937.]

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## 21. *Isotopic Exchange Reactions of Organic Compounds. Part III. Kinetics of the Isomerisation and Isotope Exchange of Vinylacetic Acid.*

By D. J. G. Ives.

The present paper is concerned with an extension of previous work (Ives and Rydon, J., 1935, 1735) on the isomerisation of vinylacetic acid to crotonic acid, with deuterium as an indicator. It has been found that the exchange reaction of vinylacetic acid proceeds faster than the isomerisation, the respective velocity constants being 0·009 and 0·0058 min.$^{-1}$, indicating that the isomerisation proceeds by a bimolecular mechanism. A kinetic proof is given that the deuterium : hydrogen ratio of the hydrogen in the α-position of the βγ-isomeride in equilibrium with the solvent is unchanged during the formation of the intermediate ions postulated by the prototropic theory of three-carbon tautomerism, a result previously deduced by other means.

On the basis of this constancy of the D/H ratio in the α-position, it has been possible to calculate the relative rates of removal from, and addition to, the vinylacetic acid molecules of protons and deuterons, the values obtained being 3·15 and 3·55 respectively, giving a value for the exchange equilibrium constant of 0·89.

In Part I (Ives and Rydon, J., 1935, 1735) it was shown that the isomerisation of vinylacetic acid in presence of aqueous alkali was accompanied by a hydrogen-exchange reaction. Although this qualitative result was of interest in so far as it excluded any intramolecular mechanism for three-carbon tautomerism, it left open the more important questions of the number of hydrogen atoms taking part in the exchange reaction, the

exchange equilibrium constant, and the rate of the reaction relative to that of isomerisation. These questions are now discussed.

For a determination, *ab initio*, of the equilibrium constant of, and the number of atoms involved in, a given exchange reaction, experiments must be carried out with "heavy" solvents covering substantially the complete range of deuterium concentrations; calculation indicates that any less variation in the deuterium content of the solvent will not provide results of any certainty. The difficulty of the problem in the present case is further increased by the isomerisation of the system during the exchange reaction; at any given time after the commencement of the reaction, the system is a mixture of a substance which does exchange with one that does not (the exchange reaction of crotonic acid is extremely slow, see Part I, *loc. cit.*). An experimental investigation of this point has not, therefore, been undertaken, but there can be no real doubt that in vinylacetic acid only the α-hydrogen atoms are involved in the exchange reaction, both on general grounds, and by comparison with the results described in the previous paper: with the possible exception of phenylacetic acid, none of the acids there studied shows more than a negligible rate of exchange in comparison with vinylacetic acid, of which the α-hydrogens only are unique.

The present work is therefore confined to the rate comparison of the two reactions and the evaluation of the isotopic discrimination factor of the exchange reaction, which also involves a knowledge of the relative rates of addition to, or removal from, the molecule of protons and deuterons.

The experimental conditions were the same as those used in Part I (*loc. cit.*), *viz.*, treatment with 1·05 mols. of N-sodium hydroxide at 100°. The results are shown in Table I, where $E$ is the exchange number (= apparent number of hydrogen atoms exchanged, on the assumption of no isotopic discrimination) and $k$ is the velocity constant of the isomerisation in minutes$^{-1}$, calculated on the assumption of 100% αβ at equilibrium.

TABLE I.

| Time, mins. | 15 | 30 | 45 | 60 | 90 | 120 | 180 | 240 | 360 | 480 |
|---|---|---|---|---|---|---|---|---|---|---|
| $E$ | 0·265 | 0·376 | 0·563 | 0·649 | 0·814 | 0·877 | 0·934 | 0·921 | 0·900 | 0·847 |
| αβ, % | 10·5 | 16·0 | 19·0 | 26·0 | 41·0 | 52·0 | — | — | — | — |
| $10^4k$, mins.$^{-1}$ | 73·7 | 58·0 | 46·9 | 50·1 | 58·6 | 61·2 | | Mean = 58 | | |

It is clear that the exchange reaction is faster than, and cannot, therefore, be entirely dependent on, the isomerisation: the intermediate ions postulated by Ingold, Shoppee, and Thorpe's theory of prototropic change (J., 1926, 1477) must therefore be kinetically free in this case, and the isomerisation must proceed by the bimolecular mechanism (cf. Hsü, Ingold, and Wilson, J., 1935, 1778). It is interesting to compare the present results with those of Ingold, de Salas, and Wilson (J., 1936, 1328) on the isomerisation and deuterium exchange of *cyclo*hexylideneacetonitrile: the present case differs in that the exchange reaction of the βγ-isomeride is not instantaneous, but is similar in that the deuterium content of the solute first rises to a maximum and then decreases. The explanation for this decrease which has been advanced by these authors applies equally well to the system now considered, but requires some further elucidation.

We consider first vinylacetic acid in deuterium equilibrium with the solvent, neglecting the isomerisation for the time being. α-Hydrogen and α-deuterium atoms are removed as protons and deuterons, respectively, by the basic hydroxyl ions present in the solvent, and are returned by the acid water molecules. The relative rates of removal and addition of protons and deuterons are, however, different, and the equilibrium ratio of deuterium to hydrogen, D/H, in the exchangeable position in the vinylacetic acid will be given by the quotient $f_2x/f_1$, where $f_2$ is the ratio of the rate of removal of protons to that of deuterons, $f_1$ is the ratio of the rates of addition of protons and deuterons, and $x$ is the ratio of deuterium to hydrogen in the solvent; $f_1$ and $f_2$ are both considerably greater than unity and $f_1$ is greater than $f_2$.

We now consider the process of isomerisation. Ingold, de Salas, and Wilson (*loc. cit.*) state that the D/H ratio for the hydrogen in the α-position of the intermediate ion (and therefore for the hydrogen in the α-position in the αβ-isomeride) must be the same as in the βγ-isomeride, where it is governed by an equilibrium. On isomerisation, a proton or

a deuteron is added ***irreversibly*** in the $\gamma$-position of the ion, and consequently, the D/H ratio of the hydrogen in the $\gamma$-position of the $\alpha\beta$-isomeride is governed by an irreversible process and not by an equilibrium, and will therefore be poorer in deuterium by an amount commensurate with the difference between $1/f_1$ and $f_2/f_1$. The decrease in the deuterium content of the solute which occurs during isomerisation is therefore explained.

This explanation depends on the identity of the D/H ratio of the hydrogen in the $\alpha$-position of the ions with that in the $\alpha$-position of the parent molecules, which follows from the fact that exchange equilibria are determined by the vibration frequencies of the links involved, which are only slightly constitutive. The ions themselves are not, of course, in direct equilibrium with the solvent (this would involve the formation of a doubly charged anion, the original charge on the carboxyl group being neglected), but it is clear thermodynamically that this is immaterial : the D/H ratio of the ions must be the same, whether their equilibrium with the solvent is direct or indirect. It has been found, however, that the exchange equilibrium constant of vinylacetic acid is 0·89, whereas the corresponding constant for *cyclo*hexylideneacetonitrile found by Ingold, de Salas, and Wilson (*loc. cit.*) is 0·67. This raises some doubt as to how far exchange equilibria involving C–H and O–H links are independent of constitution, and therefore within what limit the D/H ratios of the hydrogen in the $\alpha$-positions of the ions and molecules are identical. In order to obtain more insight into the mechanism by which this identity might be established, it was thought worth while to examine this point on a kinetic basis, and at first sight it appeared difficult to confirm this identity : for example, if protons are removed from the molecules faster than deuterons, it would appear that the resulting ions must contain relatively more deuterium than the parent molecules. The reversal of this ionisation is also governed by a discrimination factor which appears to operate in the same sense. It would also seem to be erroneous to postulate an irreversible addition (governed by the partition factor $1/f_1$ without a previous irreversible removal (governed by the factor $f_2$), unless the molecule is to accumulate a hydrogen atom extra to the number usually allowed by the rules of valency. The net effect on the total deuterium content of the solute of these *two* irreversible processes might be supposed to be the same as that of the original equilibrium. These arguments, however, are fallacious because they overlook the statistical factors involved, which are now considered.

For simplicity, we take a case in which the solvent (in infinite excess) is alcohol, containing only one exchangeable hydrogen atom per molecule. The possible equilibria between the $\beta\gamma$-molecules and ions of varying degrees of deuteration may be decomposed into the following reactions, each of which must be given equal statistical weight, and to which velocity constants may be ascribed. We again ignore the complication of isomerisation, which is permissible, since we are considering the equilibrium between ions and $\beta\gamma$-molecules only.

$$\left.\begin{array}{l} \dot{:}CH_2 + Et\bar{O} \longrightarrow \dot{:}\bar{C}H + EtOH \\ \dot{:}CH_2 + Et\bar{O} \longrightarrow \dot{:}\bar{C}H + EtOH \\ \dot{:}CHD + Et\bar{O} \longrightarrow \dot{:}\bar{C}D + EtOH \end{array}\right\} \text{Removal of H : velocity const., } k_{iH}.$$

$$\left.\begin{array}{l} \dot{:}CHD + Et\bar{O} \longrightarrow \dot{:}\bar{C}H + EtOD \\ \dot{:}CD_2 + Et\bar{O} \longrightarrow \dot{:}\bar{C}D + EtOD \\ \dot{:}CD_2 + Et\bar{O} \longrightarrow \dot{:}\bar{C}D + EtOD \end{array}\right\} \text{Removal of D : velocity const., } k_{iD}.$$

$$\left.\begin{array}{l} \dot{:}\bar{C}H + EtOH \longrightarrow \dot{:}CH_2 + Et\bar{O} \\ \dot{:}\bar{C}D + EtOH \longrightarrow \dot{:}CHD + Et\bar{O} \end{array}\right\} \text{Addition of H : velocity const., } k_{aH}.$$

$$\left.\begin{array}{l} \dot{:}\bar{C}H + EtOD \longrightarrow \dot{:}CHD + Et\bar{O} \\ \dot{:}\bar{C}D + EtOD \longrightarrow \dot{:}CD_2 + Et\bar{O} \end{array}\right\} \text{Addition of D : velocity const., } k_{aD}.$$

The reactions of removal of H or D from the molecules $\dot{:}CH_2$ and $\dot{:}CD_2$ respectively have been duplicated to emphasise that a statistical factor of 2 applies to these reactions. It is clear, for example, that the probability that a $\dot{:}\bar{C}H$ ion will be produced from $\dot{:}CH_2$ at the moment of attack by the base is double the probability that a $\dot{:}\bar{C}H$ ion will be produced from $\dot{:}CHD$ in similar circumstances, quite apart from any consideration of the relative ease of removal of H or D.

When the system is in equilibrium, the rate of formation of each of the species present, molecules or ions, must be equal to the rate of its disappearance. We can therefore set up the following equations, which must be true at equilibrium.

$$k_{aH}[\dot{:}\bar{C}H][EtOH] = 2k_{iH}[\dot{:}CH_2][Et\bar{O}] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$k_{aH}[\dot{:}\bar{C}D][EtOH] + k_{aD}[\dot{:}\bar{C}H][EtOD] = k_{iH}[\dot{:}CHD][Et\bar{O}] + k_{iD}[\dot{:}CHD][Et\bar{O}] \; . \quad (2)$$

$$k_{aD}[\dot{:}\bar{C}D][EtOD] = 2k_{iD}[\dot{:}CD_2][Et\bar{O}] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$2k_{iH}[\dot{:}CH_2][Et\bar{O}] + k_{iD}[\dot{:}CHD][Et\bar{O}] = k_{aH}[\dot{:}\bar{C}H][EtOH] + k_{aD}[\dot{:}\bar{C}H][EtOD] \; . \quad (4)$$

$$k_{iH}[\dot{:}CHD][Et\bar{O}] + 2k_{iD}[\dot{:}CD_2][Et\bar{O}] = k_{aH}[\dot{:}\bar{C}D][EtOH] + k_{aD}[\dot{:}\bar{C}D][EtOD] \; . \quad (5)$$

From equations (3) and (5) we obtain

$$k_{iH}[\dot{:}CHD][Et\bar{O}] = k_{aH}[\dot{:}\bar{C}D][EtOH] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

and from equations (1) and (4),

$$k_{iD}[\dot{:}CHD][Et\bar{O}] = k_{aD}[\dot{:}\bar{C}H][EtOD] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

Eliminating $[\dot{:}\bar{C}H]$ from equations (1) and (7), and $[\dot{:}\bar{C}D]$ from equations (3) and (6), we obtain

$$2k_{aD}k_{iH}[EtOD][Et\bar{O}][\dot{:}CH_2] = k_{aH}k_{iD}[EtOH][Et\bar{O}][\dot{:}CHD] \quad . \quad . \quad . \quad (8)$$

and

$$k_{aD}k_{iH}[EtOD][Et\bar{O}][\dot{:}CHD] = 2k_{aH}k_{iD}[EtOH][Et\bar{O}][\dot{:}CD_2] \quad . \quad . \quad . \quad (9)$$

Adding equations (8) and (9), and cancelling $[Et\bar{O}]$ throughout, we have

$$2k_{aD}k_{iH}[EtOD][\dot{:}CH_2] + k_{aD}k_{iH}[EtOD][\dot{:}CHD] = k_{aH}k_{iD}[EtOH][\dot{:}CHD] + 2k_{aH}k_{iD}[EtOH][\dot{:}CD_2] \quad (10)$$

Rearranging,

$$k_{aD}k_{iH}[EtOD](2[\dot{:}CH_2] + [\dot{:}CHD]) = k_{aH}k_{iD}[EtOH]([\dot{:}CHD] + 2[\dot{:}CD_2])$$

Hence,

$$([\dot{:}CHD] + 2[\dot{:}CD_2])/(2[\dot{:}CH_2] + [\dot{:}CHD]) = k_{aD}k_{iH}[EtOD]/k_{aH}k_{iD}[EtOH] \; . \quad (11)$$

which gives the D/H ratio of the $\alpha$-hydrogen in the $\beta\gamma$-molecules.

The D/H ratio of the $\alpha$-hydrogen in the ions is given directly by equations (6) and (7):

$$\frac{[\dot{:}\bar{C}D]}{[\dot{:}\bar{C}H]} = \frac{k_{iH}[Et\bar{O}][\dot{:}CHD]}{k_{aH}[EtOH]} \times \frac{k_{aD}[EtOD]}{k_{iD}[Et\bar{O}][\dot{:}CHD]} = \frac{k_{aD}k_{iH}[EtOD]}{k_{aH}k_{iD}[EtOH]} \quad . \quad . \quad (12)$$

which is identical with equation (11).

Substituting $k_{iH}/k_{iD} = f_2$, $k_{aH}/k_{aD} = f_1$, and $[EtOD]/[EtOH] = x$, we obtain the relationship previously stated, that the D/H ratio of the $\alpha$-hydrogen in the $\beta\gamma$-molecules (and therefore in the ions) is $f_2x/f_1$. Equation (2) has not been used in this proof, but it

is obviously satisfied by the results. It can also be shown that the equivalence between the deuterium contents of the ions and molecules holds, even when the system has not reached equilibrium.

In the case of water as solvent, a general treatment on these lines would be more complex, but it is clear that the same proof will approximately apply in the case of dilute deuterium water.

We now analyse the vinylacetic acid results. The processes which occur in the system may be symbolised by means of the following scheme:

$$\begin{aligned} &A \longrightarrow B, \text{ with velocity const. } k_1 \\ &A \longrightarrow C, \text{ with velocity const. } k_2 \\ &B \longrightarrow D, \text{ with velocity const. } k_3 \end{aligned}$$

where A is "light" vinylacetic acid, B is vinylacetic acid in deuterium equilibrium with the solvent, C is crotonic acid produced by isomerisation of A (and therefore deuterated in the $\gamma$-position only), D is crotonic acid produced by isomerisation of B, and $k_1$, $k_2$, and $k_3$ are the respective pseudo-unimolecular velocity constants of these reactions.

It can be shown as follows that $k_2$ and $k_3$ are identical. Hydrogen, or deuterium, will add on to the ion $CH_2{=}CH{-}\bar{C}H{-}CO_2H$ at exactly the same rate as it adds on to the ion $CH_2{=}CH{-}\bar{C}D{-}CO_2H$; there is no reason to suppose that the initial presence of deuterium in an ion, instead of hydrogen, in any way affects the subsequent addition of hydrogen or deuterium. The rate of disappearance of "heavy" vinylacetic acid is therefore identical with the rate of disappearance of "light" vinylacetic acid, *i.e.*, $k_2 = k_3$, and the remaining system of vinylacetic acid remains unaltered in its "deuterium specification" whilst decreasing in size. Further, in the scheme

$$\beta\gamma\text{-molecules} \rightleftharpoons \text{ions} \longrightarrow \alpha\beta\text{-molecules}$$

the second stage is to all intents and purposes irreversible (see preceding paper) and is the rate-controlling step of the isomerisation; $k_2$ may therefore be equated to the experimentally determined rate of isomerisation.

The quantities $k_1$, $f_1$, and $f_2$ can now be calculated as follows. Let $a$ = initial concentration of A, $y$ = concentration of A at time $t$, and $x$ = concentration of B at time $t$. Then the rate of loss of A is given by

$$dy/dt = k_1y + k_2y \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

$$\therefore y = ae^{-(k_1+k_2)t} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

and the rate of formation of B by

$$dx/dt = k_1y - k_2x = k_1ae^{-(k_1+k_2)t} - k_2x \quad . \quad . \quad . \quad . \quad . \quad (15)$$

$$\therefore dx/dt + k_2x = ak_1e^{-(k_1+k_2)t} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$

Multiplying both sides by $e^{k_2t}$, we obtain,

$$(dx/dt)e^{k_2t} + k_2x \,.\, e^{k_2t} = ak_1e^{-k_1t} \quad . \quad . \quad . \quad . \quad . \quad . \quad (17)$$

or

$$(dx/dt)e^{k_2t} + x[d(e^{k_2t})/dt] = ak_1e^{-k_1t}$$

The left-hand side of this equation is now a perfect differential: integrating, we obtain $x \,.\, e^{k_2t} = -ae^{-k_1t} + I$, where $I$ is an integration constant which can be evaluated, since when $t = 0$, $x = 0$; therefore

$$x = ae^{-k_2t}(1 - e^{-k_1t}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (18)$$

The further quantities required are the concentrations of C and D. Let these have the values $m$ and $n$ respectively at time $t$. Then the rate of formation of C is given by

$$dm/dt = k_2y = k_2ae^{-(k_1+k_2)t} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (19)$$

and on integration we obtain

$$m = ak_2[1 - e^{-(k_1+k_2)t}]/(k_1 + k_2) \quad . \quad . \quad . \quad . \quad . \quad . \quad (20)$$

The concentration of (C + D) at time $t$ is clearly given by

$$m + n = a(1 - e^{-k_2 t}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (21)$$

and hence,
$$n = a(1 - e^{-k_2 t}) - ak_2[1 - e^{-(k_1 + k_2)t}]/(k_1 + k_2) \quad . \quad . \quad . \quad . \quad (22)$$

Equations (18), (20), and (22) provide a means of calculating the concentrations of B, C, and D at time $t$ in terms of $k_1$ and $k_2$; $k_1$, the velocity constant of the exchange reaction of vinylacetic acid, is unknown, but may be estimated in the following way. At any time, the deuterium in the mixed solute (expressed in terms of exchange numbers) will be arranged thus:

$$\begin{cases} 2xf_2/f_1 \text{ atoms in } x \text{ mols of B} \\ m/f_1 \text{ atoms in } m \text{ mols of C (in the } \gamma\text{-position)} \\ nf_2/f_1 + n/f_1 \text{ atoms in } n \text{ mols of D (in the } \alpha\text{- and } \gamma\text{-positions, respectively)} \end{cases}$$

The sum of these quantities may be equated to the total exchange number, determined experimentally:

$$2xf_2/f_1 + m/f_1 + nf_2/f_1 + n/f_1 = E \quad . \quad . \quad . \quad . \quad . \quad . \quad (23)$$

and hence
$$(m + n)/E = f_1 - f_2(2x + n)/E \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (24)$$

Since $f_1$ and $f_2$ are constants (cf. Ingold, de Salas, and Wilson, *loc. cit.*), this expression must be linear, and we therefore choose the value of $k_1$ which satisfies this condition.

Fig. 1.

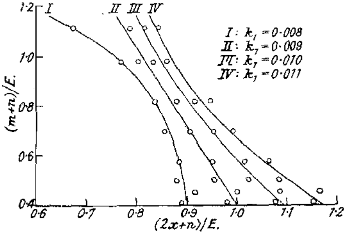
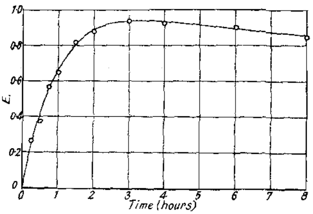



Fig. 2.




Values of $(m + n)/E$ and $(2x + n)/E$ have been calculated for $k_2 = 0{\cdot}0058$ (see Table I) and for various assumed values of $k_1$ and are plotted in Fig. 1. The first two experimental points have been neglected owing to the greater probable error in the time factor.

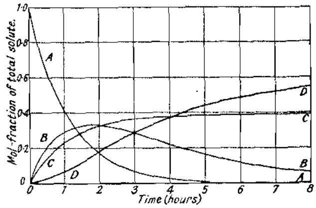
The value $k_1 = 0{\cdot}009$ has been selected as giving the best straight line, although the error in this estimation may be $\pm\, 0{\cdot}001$. The method of least squares then gives the values $f_1 = 3{\cdot}55$, $f_2 = 3{\cdot}15$, and hence $f_2/f_1 = 0{\cdot}89$. In order to check these results, theoretical exchange numbers have been calculated and compared with the observed values: this comparison is shown in Table II and graphically in Fig. 2, where the continuous line indicates the theoretical values and the circles the experimental values. The agreement is evidently well within experimental error over the whole range.

Table II.

| Time, mins. | 15 | 30 | 45 | 60 | 90 | 120 | 180 | 240 | 360 | 480 |
|---|---|---|---|---|---|---|---|---|---|---|
| $E$, calc. | 0·234 | 0·416 | 0·556 | 0·664 | 0·806 | 0·884 | 0·937 | 0·933 | 0·891 | 0·859 |
| $E$, obs. | 0·265 | 0·376 | 0·563 | 0·649 | 0·814 | 0·877 | 0·934 | 0·921 | 0·900 | 0·847 |
| Diff. $\times 10^3$ | +31 | −40 | +7 | −15 | +8 | −7 | −3 | −12 | +9 | −12 |

It is of interest to plot the changing amounts of the various species during the course of the isomerisation and exchange reactions, as an aid to visualising the course of events: this has been done in Fig. 3, in terms of mol.-fractions of the total solute.

Fig. 3.




A = "light" vinylacetic acid.
B = *vinylacetic acid in deuterium equilibrium with solvent.*
C = *crotonic acid from isomerisation of* A (*deuterated in γ-position only*).
D = *crotonic acid from isomerisation of* B.

## Experimental.

*Preparation of Materials.*—Vinylacetic acid was prepared by Linstead, Noble, and Boorman's method (J., 1933, 560) and redistilled before use, b. p. 79°/20 mm. (Found: equiv., by titration, 86·1. Calc.: 86·05). The other materials were prepared exactly as described in the previous paper.

*Equilibration Experiments.*—The exchange experiments and isotopic analyses of solvents and solutes were performed as described in the previous paper. For the estimation of isomerides, a separate series of equilibrations in a solvent of normal isotopic composition was carried out under closely similar conditions: it was assumed that the alteration in the rate of isomerisation due to the presence of 2·5% of deuterium oxide in the solvent would be negligible. The mixed acids were isolated in the usual manner and analysed by the bromometric method of Linstead and Noble (J., 1934, 617), a reference curve being obtained from synthetic mixtures of the pure isomerides.

The author wishes to record his thanks to Prof. S. Sugden, F.R.S., Prof. C. K. Ingold, F.R.S., and Dr. C. L. Wilson for helpful discussions, and to Dr. H. N. Rydon for help and advice in connexion with the experimental work.

Birkbeck College, London, E.C. 4. [*Received, October 20th*, 1937.]

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# 22. *The Synthesis of* r-6-*Methoxytryptophan and of Harmine, with a Note on the Action of Acetaldehyde on Tryptophan.*

By Douglas Graham Harvey and William Robson.

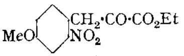
The synthesis of r-6-*methoxytryptophan*, which may be regarded as the biological precursor of the *Harmala* alkaloids, has been effected. Attempts to demethylate the new amino-acid have been unsuccessful and it would appear that before the hydroxy-derivative can be obtained a new method of synthesising tryptophan will be necessary. It is shown that acetaldehyde will condense with tryptophan in aqueous solution at the ordinary temperature to form 3-methyl-3 : 4 : 5 : 6-tetrahydro-4-carboline-5-carboxylic acid, this substance being identified by its oxidation to harman. The corresponding 6-methoxy-derivatives have also been studied.

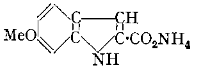
The researches of Kermack, Perkin, and Robinson (J., 1921, **119**, 1617), who showed that harman is produced by the oxidation of the reaction product of *l*-tryptophan and acetaldehyde, of Spath and Lederer (*Ber.*, 1930, **63**, 112), who transformed acetyl-6-methoxytryptamine into harmaline, and of Akabori and Saito (*ibid.*, p. 2245), who condensed tryptamine with acetaldehyde to obtain tetrahydroharman, would almost certainly indicate that the amino-acids 6-hydroxytryptophan and its corresponding methoxy-derivative are the biological precursors of the *Harmala* alkaloids.

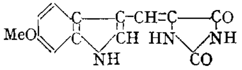
The possible occurrence of 6-hydroxytryptophan in the plant has been mooted by Barger (*Ann. Reports*, 1919, **157**); that it may have even wider distribution in nature is suggested by the communication of Abderhalden and Baumann (*Z. physiol. Chem.*, 1908, **55**, 412) on the presence of an unidentified hydroxytryptophan in a tryptic digest of casein. Nothing, however, is known of these amino-acids and since their isolation and

the study of their properties would help to clarify our knowledge regarding the mode of formation of the alkaloids *in vivo*, and moreover, yield data facilitating a search for the amino-acids themselves in plant and animal products, it was decided to attempt their synthesis. The present communication deals with the synthesis of *6-methoxytryptophan* and its transformation into harmine. At one time it was hoped that demethylation of the former compound would yield the required hydroxy-amino-acid. Up to the present, however, efforts in this direction have proved unavailing and a new line of attack would appear essential.

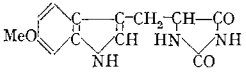
6-Methoxyindole, which was described by Kermack, Perkin, and Robinson (*loc. cit.*) in their attempt to obtain 6-methoxytryptophan, has now been prepared as follows: *o*-Nitro-*p*-toluidine was converted through *o*-nitro-*p*-cresol (Manske, " Organic Syntheses," 396) into *o*-nitro-*p*-tolyl methyl ether (cf. Kermack, Perkin, and Robinson, *loc. cit.*), which was condensed with ethyl oxalate in dry ether in the presence of potassium ethoxide (Wislicenus and Thoma, *Annalen*, 1924, **436**, 24; Blaikie and Perkin, J., 1924, **125**, 296). The resulting unstable potassio-derivative of ethyl *o*-nitro-*p*-methoxyphenylpyruvate (I)

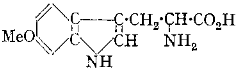

(I.)


(II.)


(III.)

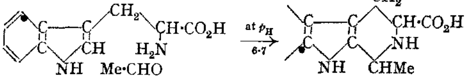
was converted into ammonium 6-methoxyindole-2-carboxylate (II) in excellent yield by dissolving it, immediately it was isolated, in cold water and after 15 minutes treating the filtered solution with ferrous sulphate and ammonia. Decarboxylation of the product proceeded most satisfactorily in hot glycerol, and 6-methoxyindole-3-aldehyde was then obtained by Boyd and Robson's modification (*Biochem. J.*, 1935, **29**, 555) of the Ellinger–Reimer–Tiemann method. The remaining stages closely followed the hydantoin method of synthesising amino-acids as modified by Boyd and Robson (*Biochem. J.*, 1935,

(IV.)



(V.)

**29**, 542, 546). Condensation of the aldehyde with hydantoin was effected in boiling piperidine, and the reduction of the resulting 5-(*6'-methoxyindolal*)*hydantoin* (III) accomplished by treating a solution of it in pyridine with hydrogen sulphide at 100° for 70 hours. Cleavage of the saturated *hydantoin* (IV) by heating it in an ammoniacal solution at 100° gave the required 6-methoxytryptophan (V) in good yield and purity.

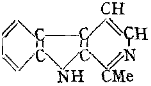
Before the conversion of the amino-acid to the " alkaloidal " stage was attempted, an investigation of the best conditions for the condensation of acetaldehyde and tryptophan was carried out. Kermack, Perkin, and Robinson (*loc. cit.*) in their synthesis of harman mixed these substances in dilute acid solution and obtained their product by immediately oxidising the mixture. Akabori and Saito (*loc. cit.*) and Hahn and his co-workers (*Ber.*, 1934, **67**, 2031; *Annalen*, 1935, **520**, 107) studied the effect of buffered solutions on the " biological " condensation of tryptamine hydrochloride with various aldehydic and ketonic compounds, and Jacobs and Craig (*J. Biol. Chem.*, 1936, **11**, 759) in their investigation into the constitution of lysergic acid condensed *l*-tryptophan with various aldehydes, again in acid solution. It is now found that, if a molar quantity of freshly distilled acetaldehyde is added to a cold saturated aqueous solution of *l*-tryptophan

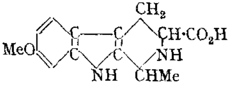

(VI.)

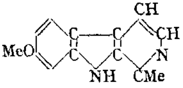
$p_H$ 6·7) and the mixture is kept overnight at room temperature, 3-methyl-3 : 4 : 5 : 6-etrahydro-4-carboline-5-carboxylic acid (VI) separates. Evaporation of the mother-liquor

and addition of alcohol to the concentrate gives a further crop of the carboline, the yield becoming quantitative.

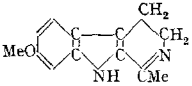
From the ease with which this reaction takes place it would appear that we were approaching the "biological" conditions under which the formation of the alkaloids takes place *in vivo*. At the moment, however, we do not attach much importance to the reaction, for the following reasons. Treatment of the carboline derived from

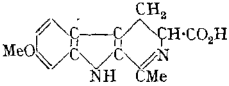

(VII.)


(VIII.)


(IX.)

tryptophan with the most gentle oxidising agents yielded harman (VII) in 70% yield, whereas the corresponding 11-*methoxy-carboline* (VIII) yielded harmine (IX) in only a 40% yield. It would appear, then, that the presence of the methoxy-group effects some difference in the behaviour of the carbolines towards oxidising agents, although no evidence has been obtained of a compound resembling harmaline (X) or 11-methoxy-3-methyl-5 : 6-dihydro-4-carboline-5-carboxylic acid (XI) in the reaction mixture. Moreover,

(X.) 

 (XI.)

attempts to decarboxylate 3-methyl-3 : 4 : 5 : 6-tetrahydro-4-carboline-5-carboxylic acid by the methods available for the degradation of amino-acids to amines have been unsuccessful and this would seem to indicate that the tetrahydropyridine ring is formed after, rather than before, decarboxylation has occurred; in other words, the amine and not the amino-acid may be the precursor of these alkaloids in the plant.

## Experimental.

o-*Nitro*-p-*cresol*.—The suspension obtained by cooling a solution of *o*-nitro-*p*-toluidine (100 g.) in warm 10% sulphuric acid (1500 ml.) to 0° was diazotised with sodium nitrite (50 g. in water, 130 ml.) (cf. Manske, *loc. cit.*), added during 20 minutes, and the red mixture cautiously added to boiling dilute sulphuric acid (1000 ml. of conc. acid in water, 2000 ml.). When the tar had coagulated, the yellow solution was rapidly cooled. The cresol, collected next day, crystallised from water in large yellow needles, m. p. 77—78° (yield, 55—60%).

o-*Nitro*-p-*tolyl Methyl Ether*.—To a well-cooled solution of *o*-nitro-*p*-cresol (75 g.) in aqueous caustic soda (30 g. in 220 ml. of water), methyl sulphate (100 ml.) was added in 10 ml. portions, the temperature being kept below 50°. The solution was then heated on the water-bath until the red colour had practically disappeared (15 minutes), excess of caustic soda added (25 g. in 100 ml. of water), and the whole heated on the water-bath for 5 minutes. A washed and dried ethereal extract of the product gave on distillation a fraction, b. p. 150°/20 mm., as a pale yellow, viscous liquid consisting of practically pure *o*-nitro-*p*-tolyl methyl ether (yield, 90—95%); this rapidly solidified in needles (m. p. 15·5°) when cooled in ice.

*Potassium Derivative of Ethyl* o-*Nitro*-p-*methoxyphenylpyruvate* (I).—A suspension of potassium ethoxide prepared from potassium (7·8 g.) and dry alcohol (15 ml.) in dry ether was well cooled, and ethyl oxalate (29·2 g.) slowly added with vigorous shaking, followed, after cooling in ice–salt for 20 minutes, by an ethereal solution of *o*-nitro-*p*-tolyl methyl ether (33·4 g.), added in 10 ml. portions without rise in temperature. The dark red solution was kept at room temperature for 48 hours, and the crystalline potassium derivative then collected, washed with ether, and immediately treated as described in the next section (yield, 70—80%).

*Ammonium 6-Methoxyindole-2-carboxylate* (II).—A solution of the potassium derivative (100 g.) in water (1000 ml.) was after 15 minutes extracted with ether, filtered, and diluted to 1500 ml. with water, and 80 ml. of aqueous ammonia (*d* 0·880) added, followed by a hot

solution of ferrous sulphate (900 g. in 1300 ml. of water). The whole was warmed for ½ hour, boiled for ½ hour, and filtered hot, the ferric oxide sludge washed with hot water, and the combined filtrate and washings concentrated; ammonium 6-methoxyindole-2-carboxylate (pale pink plates) was obtained in 50—60% yield.

6-*Methoxyindole*.—The preceding salt (7·5 g.) was carefully heated in glycerol for 2—3 hours at 200—210°, the mass poured into water and cooled at 0° for 6 hours, and the indole recrystallised from hot ligroin, forming plates (3·9 g.), m. p. 92°.

6-*Methoxyindole-3-aldehyde*.—A boiling solution of 6-methoxyindole (15 g.) in 96% alcohol (300 ml.) and chloroform (115 ml.) was treated with a solution of potassium hydroxide (150 g. in 180 ml. of water) at such a rate that a steady but not too vigorous reaction was maintained. The solution was boiled for a further 4 hours and kept at room temperature overnight. The potassium chloride was then removed and washed with 96% alcohol, and the washings and filtrate steam-distilled. After the alcohol and chloroform had passed over, the receiver was changed and the distillation continued for a further 20 hours, by which time all the unchanged 6-methoxyindole and 3-chloro-7-methoxyquinoline had distilled. The hot liquor in the flask was filtered from the coagulated tar and set aside to cool. The tar was dissolved in alcohol, the solution poured into water, the alcohol removed by steam-distillation, and the resulting mixture filtered. The filtrate deposited a further crop of aldehyde. The remaining tar was submitted to the same process a second time. The yellow needles of 6-methoxyindole-3-aldehyde which separated from all the solutions were combined and recrystallised from hot water; they were then obtained practically colourless. Yield, 4·5 g. or 25% of the theoretical. The aldehyde (Found: N, 8·2. Calc.: N, 8·0%) had m. p. 186° (Kermack, Perkin, and Robinson give 186°) and gave a slight colour with Ehrlich's reagent and a deep pink colour with warm 50% sulphuric acid.

3-*Chloro-7-methoxyquinoline*.—The steam-distillate from the above preparation was shaken six times with ether, and the extracts concentrated and shaken several times with small quantities of dilute acid. The acid washings were made alkaline with 10% caustic soda solution, and the 3-chloro-7-methoxyquinoline collected and recrystallised from 50% alcohol. It had a pleasant smell characteristic of the substituted 3-chloroquinolines and melted at 93—94°. Yield, 2 g. from 15 g. of 6-methoxyindole.

5-(6'-*Methoxyindolal*)*hydantoin* (III).—6-Methoxyindole-3-aldehyde (3·5 g.), hydantoin (2·3 g.; 1·2 mols.), and freshly distilled piperidine (10 ml.) were heated under reflux for 35 minutes, a bright yellow, crystalline solid beginning to separate after 15 minutes. The resulting semi-solid mass was poured into water and made slightly acid with acetic acid, the liquid filtered, and the solid collected, washed with methyl alcohol and with hot water, and recrystallised from pyridine–water and also from glacial acetic acid, forming stout yellow prisms or blunt needles (3·7 g.) of 5-(6'-*methoxyindolal*)*hydantoin*, m. p. 311—315° (Found: N, 16·5. $C_{13}H_{11}O_3N_3$ requires N, 16·3%). It was practically insoluble in absolute ethyl and methyl alcohols, ether, benzene, xylene and ligroin and gave, when heated with Ehrlich's reagent, a very pale pink colour which faded rapidly on cooling.

5-(6'-*Methoxyindolylmethyl*)*hydantoin* (IV).—A solution of 6'-methoxyindolalhydantoin (1·0 g.) in pyridine (20 ml.) was saturated with hydrogen sulphide at 0° and heated in a closed bottle at 100° for 21 hours; fresh pyridine was then added (20 ml.), and the process of saturation with hydrogen sulphide and heating repeated. The pyridine was finally removed in a vacuum, and the residue treated with 100 ml. of absolute alcohol. The alcoholic solution was filtered (the unchanged 6'-methoxyindolalhydantoin only amounted to 0·1—0·2 g.), diluted to 200 ml. with water, boiled with a little animal charcoal, and again filtered. The filtrate on standing deposited 0·45 g. of practically colourless 5-(6'-*methoxyindolylmethyl*)-*hydantoin*. This, on recrystallisation from 50% alcohol, formed large plates, m. p. 220° (Found: N, 16·1. $C_{13}H_{13}O_3N_3$ requires N, 16·2%). Yield (based on recovered unreduced hydantoin), 50%.

6-*Methoxytryptophan* (V).—A mixture of 6'-methoxyindolylmethylhydantoin (3·2 g.), aqueous ammonia (6 ml., *d* 0·880), and water (150 ml.) (after treatment with hydrogen sulphide for 5 minutes to prevent oxidation) was heated in a closed bottle for 72 hours at 100—110°. The solution was evaporated to dryness in a vacuum and the residue was extracted, first with alcohol to remove sulphur and unchanged hydantoin, and then with hot water to remove the amino-acid. The aqueous extract was concentrated to 20 ml. and treated with 60 ml. of absolute alcohol. The thick crust of 6-*methoxytryptophan* which formed on the surface was removed, and the filtrate concentrated to 10 ml. and treated with a further 60 ml. of absolute alcohol; a second crop of less pure amino-acid was then

precipitated, the total yield being 1·9 g. (60%). Recrystallisation from water gave well-defined hexagonal plates. Like *r*-tryptophan, the 6-methoxy-derivative was intensely sweet to the taste, and insoluble in alcohol, ether, and benzene. It darkened and shrank at 246—250°, melted at 263—268°, and frothed with charring at 274°. It gave with the Hopkins–Cole reagent a greenish-blue colour, changed by a few drops of ferric chloride solution to purplish-red; dilution with water produced a vivid green-blue solution. Bromine water gave a characteristic rose-pink colour, readily removed by amyl and butyl alcohols (Found for material dried at 110°/15 mm.: C, 61·9; H, 6·1; N, 11·9. $C_{12}H_{14}O_3N_2$ requires C, 61·5; H, 5·9; N, 12·0%).

*Attempted Demethylation of* r-6-*Methoxytryptophan.*—The tryptophan was (1) heated for 3·5 hours with 35% hydrochloric acid at 150°, (2) dissolved in dilute sulphuric acid (5 g. of acid : 5 ml. of water) and boiled under reflux for 2 hours in an atmosphere of nitrogen, (3) heated with N/10-sulphuric acid (1 mol.) for 7 hours at 160°. A dark brown, amorphous product was isolated in the first case and greenish amorphous masses in the other two.

3-*Methyl*-3 : 4 : 5 : 6-*tetrahydro*-4-*carboline*-5-*carboxylic Acid* (VI).—A solution of *l*-tryptophan (0·3 g.) in water (10 ml.) was cooled, treated with freshly distilled acetaldehyde (1 ml.), and kept in a corked bottle at room temperature overnight. Colourless opaque needles (0·2 g., m. p. 290° after preliminary darkening at 280°) had then formed, and the mother-liquor gave, on concentration and addition of a large excess of alcohol, a further crop of the carboline (yield, practically theoretical). Recrystallised from a small volume of water by the addition of alcohol, it formed practically colourless needles, m. p. 295—299° (Found for material dried at 110°/15 mm.: C, 68·6; H, 6·1; N, 12·0. Calc. for $C_{13}H_{14}O_2N_2$: C, 67·8; H, 6·1; N, 12·2%).

3-*Methyl*-4-*carboline* (*Harman*) (VII).—To a boiling solution of the preceding acid (0·25 g.) in water (65 ml.), 10% potassium dichromate solution (12·5 ml.) was added, and then glacial acetic acid (2·5 ml.). The solution was boiled for 1 minute, cooled, treated with dilute sodium sulphite solution to remove the excess of oxidising agent, made strongly alkaline with sodium carbonate, and shaken with ether. The extracts were evaporated to dryness, leaving a mass of pale yellow needles (0·152 g.), m. p. 238° after recrystallisation from alcohol (Jacobs and Craig give m. p. 238°). The base gave salts which fluoresced bright blue in aqueous alcoholic solution.

11-*Methoxy*-3-*methyl*-3 : 4 : 5 : 6-*tetrahydro*-4-*carboline*-5-*carboxylic Acid* (VIII).—*r*-6-Methoxytryptophan (0·5 g.) was dissolved in water (50 ml.), treated with acetaldehyde (1 ml.), and warmed gently for 10 minutes. The colourless hexagonal rods formed (0·42 g.) were removed, the filtrate concentrated to 1 ml., and a further crop of the *carboline* precipitated by the addition of a large excess of alcohol (yield, approximately theoretical). The carboline resembled the demethoxycarboline (m. p. 295—299°) in properties, but melted at 244—246° (Found for material crystallised from water and dried at room temperature: loss at 120°/3 mm. after 4 hours, 6·1. $C_{14}H_{16}O_3N_2,H_2O$ requires $H_2O$, 6·5%. Found for material crystallised from water and air-dried: C, 62·5; H, 6·5. $C_{14}H_{16}O_3N_2$ requires C, 64·6; H, 6·2%. Found for material crystallised, in opaque yellow needles, from water by the addition of a large volume of alcohol and dried at 110°: N, 10·75. $C_{14}H_{16}O_3N_2$ requires N, 10·8%).

11-*Methoxy*-3-*methyl*-4-*carboline* (*Harmine*) (IX).—The above carbolinecarboxylic acid (0·1 g.) was oxidised in the same way as the acid (VI) (water, 30 ml.; 10% potassium dichromate solution, 5·0 ml.). The residue obtained from the dried ethereal extracts was recrystallised from methyl alcohol and water, giving colourless needles of harmine, m. p. 260—261° (Found: N, 13·1. Calc. for $C_{13}H_{12}ON_2$: N, 13·2%). Yield, 40%. The base formed characteristic salts with dilute mineral acids (*e.g.*, the hydrochloride) which gave a blue fluorescence in aqueous-alcoholic solution.

Our thanks are due to Miss Agnes Shore, B.Sc., for a gift of *l*-tryptophan, and to Mr. Peter Spworth for assistance in carrying out some of the analyses. Part of the work described above was done during the tenure of a Berridge Scholarship awarded to one of us (D. G. H.) by the Delegacy of the University of London, King's College.

KING'S COLLEGE, UNIVERSITY OF LONDON. [*Received, November 30th,* 1937.]

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# 23. *Studies in the Sterol Group. Part XXXIV. The Dibromination of 6-Ketocholestanyl Acetate.*

By I. M. Heilbron, H. Jackson, E. R. H. Jones, and F. S. Spring.

With the object of preparing steroid ketones containing unsaturated centres in rings A and B [see (II), p. 103] the dibromination of 6-ketocholestanyl acetate has been investigated. Two isomeric dibromides have been isolated and characterised as 5 : 7- and 5′ : 7-dibromo-6-ketocholestanyl acetates. The reactions of these bromides with pyridine and with sodium acetate in alcohol have been examined in detail and several new unsaturated ketones characterised.

When 6-ketocholestanyl acetate is treated with two moles of bromine in ether–acetic acid at 0°, 5-bromo-6-ketocholestanyl acetate (I) (Heilbron, Jones, and Spring, J., 1937, 801) separates and remains in suspension as sole product, even after long standing. If, however, the addition is effected in acetic acid at room temperature, (I) separates immediately and then gradually redissolves. Treatment of the reaction mixture with water after 1 hour gives 5 : 7-*dibromo-6-ketocholestanyl acetate* (III), m. p. 152°, in 40% yield, and after 18 hours similar treatment gives the same yield of the isomeric 5′ : 7-*dibromo-6-ketocholestanyl acetate* (IV), m. p. 129°.

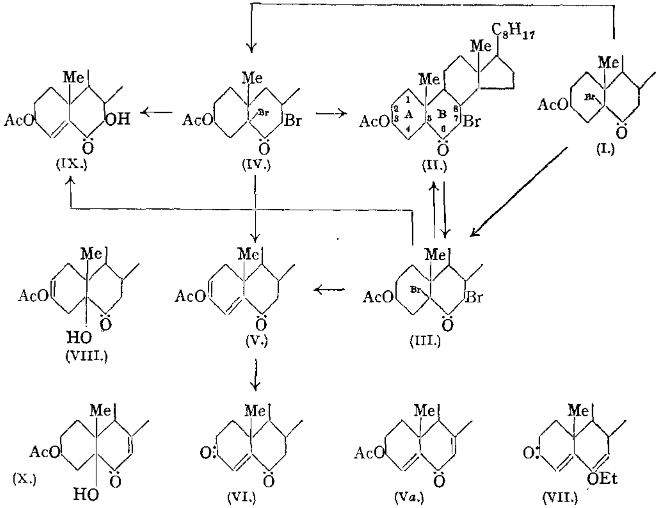
The isomeric 5- and 7-bromo-6-ketocholestanyl acetates (I) and (II) (Heilbron, Jones, and Spring, *loc. cit.*) are stable to bromine in acetic acid and chloroform under a variety of conditions and further bromination can only be effected in the presence of at least one mole of hydrogen bromide. Under suitable reaction conditions the 5-monobromide can be converted into either of the dibromides, but the 7-monobromide gives only the higher-melting isomer (III).

Since dibromination of 6-ketocholestanyl acetate gives (III) in a comparatively short time, it appeared probable that the latter is isomerised on long standing in the presence of hydrogen bromide to (IV). That this view is untenable is shown by the fact that treatment of the dibromide (III) with hydrogen bromide and acetic acid simply reduces it to 7-bromo-6-ketocholestanyl acetate (II), a reaction inhibited by the presence of bromine. Incidentally (IV) is stable to hydrogen bromide at room temperature, but at 100° it is likewise reduced to the 7-monobromide. The conversion of (I) into (III) and (IV) must thus proceed by simultaneous and not consecutive reactions, which probably involve the further bromination of an intermediate ion or radical related to 7-bromo-6-ketocholestanyl acetate. We attribute the fact that only 5′ : 7-dibromo-6-ketocholestanyl acetate (IV) can be isolated after 18 hours to the slow conversion of the less soluble isomer (III) into the very soluble 7-bromo-6-ketocholestanyl acetate (II). We have shown above that the latter reaction is inhibited by bromine and, as anticipated, we have found that treatment of 6-ketocholestanyl acetate with slightly more than two moles of bromine gives only (III) even after 24 hours.

Treatment of either of the dibromides with boiling pyridine gives two products, m. p. 139—140° and 227—229°. The former, which preponderates, has the formula $C_{29}H_{44}O_3$, and on hydrolysis with cold sodium methoxide gives 3 : 6-diketo-$\Delta^4$-cholestene (VI). Of the two possible constitutions (V) and (V*a*) for the compound, m. p. 139—140°, we favour the former (*6-keto-3-acetoxy-$\Delta^{2:4}$-cholestadiene*), since the alternative (V*a*) does not afford a ready interpretation of the behaviour on hydrolysis, nor does the compound give the Tortelli–Jaffé reaction (Heilbron and Spring, *Biochem. J.*, 1930, **24**, 133). The new enol-acetate (V) exhibits a well-defined band at 3170 A., differing from that of the enol-ether of 3 : 6-diketo-$\Delta^4$-cholestene (VII) (Butenandt and Schramm, *Ber.*, 1936, **69**, 2289), which is characterised by a band at 2950 A. This observation affords another example of the different chromophoric effect of a conjugated system according as it is present in a single cyclic system or distributed between two rings.

The product, m. p. 227—229°, has the formula $C_{29}H_{46}O_4$; its formation from either dibromide has therefore involved the elimination of one molecule of hydrogen bromide and replacement of the second halogen atom by a hydroxyl group. In view of the established constitution of the major product (V) an attractive hypothesis appeared to

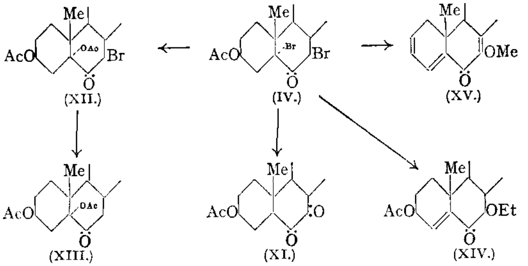
be that the second product is 5-hydroxy-6-keto-3-acetoxy-$\Delta^2$-cholestene (VIII). This is excluded, however, since on hydrolysis it fails to give either of the known 3 : 6-diketo-5-hydroxycholestanes. Of the two remaining constitutions, 7-hydroxy-6-keto-3-acetoxy-$\Delta^4$-cholestene (IX) and 5-hydroxy-6-keto-3-acetoxy-$\Delta^7$-cholestene (X), the former is correct, since the compound gives a *benzoate*, m. p. 136—137°, and does not exhibit the typical light absorption properties and Tortelli–Jaffé reaction characteristic of (X) (cf. Burawoy, J., 1937, 409).




In contrast to the reaction with boiling pyridine a marked difference is observed on reatment of the two dibromides with this reagent (or with pyridine and silver nitrate) t room temperature. Whereas the dibromide (IV) gives halogen-free mixtures from hich no crystalline product has as yet been isolated, both (III) and 5- and 7-bromo-6-etocholestanyl acetates are recovered unchanged. The dibromide (III) and the two ıonobromides are also unchanged after heating with sodium acetate in alcohol, whereas he dibromide (IV) gives a mixture from which 6 : 7-diketocholestanyl acetate (XI) has een isolated, together with two other compounds, m. p. 198° and 119—120°. The roduct, m. p. 198°, which is obtained as sole product by treatment of (IV) with potassium cetate in acetic acid, has been characterised as *7-bromo-6-keto-3 : 5′-diacetoxycholestane* XII), since on treatment with aluminium amalgam it gives a 6-keto-3 : 5-diacetoxy-ıolestane (XIII), m. p. 169°, the identity of which was established by comparison with ı authentic specimen prepared by the method of Schenck (*Z. physiol. Chem.*, 1936, **243**, 19). An interesting stereochemical point emerges from the isolation of this diacetoxy-tone from the dibromide (IV). We have previously shown (Heilbron, Jones, and oring, *loc. cit.*) that hydrolysis of 5-bromo-6-ketocholestanyl acetate gives a 3 : 5-hydroxy-6-ketocholestane, m. p. 138°. This differs from the dihydroxy-ketone, m. p. 2°, prepared by hydrolysis of the 6-keto-3 : 5-diacetoxycholestane described above,*

* Attempts to hydrolyse the two dibromides to the corresponding trihydroxy-ketones were successful,

and consequently the two dihydroxy-ketones must differ solely in the orientation of the groups associated with $C_5$. According to the nomenclature adopted by us, the dihydroxy-ketone, m. p. 138°, will be 3 : 5- and the isomer m. p. 232°, 3 : 5′-dihydroxy-6-keto-cholestane. It proves, therefore, that the orientation of the halogen atom in 5-bromo-6-ketocholestanyl acetate relative to the angular methyl group at $C_{10}$ is the same as that of the $C_5$ halogen atom in the dibromide (III) and opposite to that in (IV), and consequently we designate (III) as 5 : 7-dibromo-6-ketocholestanyl acetate and (IV) as 5′ : 7-dibromo-6-ketocholestanyl acetate, a notation which has a relative and not an absolute significance.




The product, m. p. 119—120°, has the formula $C_{31}H_{50}O_4$; it contains an ethoxy-group and exhibits general absorption in the ultra-violet region of the spectrum (figure) similar to that shown by the unsaturated hydroxy-ketone (IX). These facts suggest the constitution *6-keto-3-acetoxy-7-ethoxy-$\Delta^4$-cholestene* (XIV) for the compound; with either cold alcoholic potassium hydroxide or a hot solution of sodium methoxide in methyl alcohol it gives *3-hydroxy-6-keto-7-ethoxy-$\Delta^4$-cholestene*, m. p. 113°.

With potassium acetate in *n*-butyl alcohol, 5′ : 7-dibromo-6-ketocholestanyl acetate yields a product which exhibits an intense ferric chloride coloration. Repeated crystallisation of this crude product from methyl alcohol gives *6-keto-7-methoxy-$\Delta^{2:4:7}$-cholestatriene* (XV), m. p. 119—121°, which shows a well-defined absorption maximum at 3150 A. The formation of this enol-ether has obviously involved the methylation of an intermediate 6 : 7-diketone, since neither the enol-ether nor the material recovered from the combined mother-liquors gives any reaction with ferric chloride.

## Experimental.

Great difficulty has been experienced in the preparation of 6-ketocholestanyl acetate according to the directions available in the literature. A method which we have developed and found suitable for the preparation of relatively large quantities of the saturated keto-acetate is appended. A suspension of cholesterol (20 g.) in acetic acid (80 c.c.) was treated with 30 drops of a mixture of nitric acid (80 c.c.; *d* 1·50) and fuming nitric acid (50 c.c.; Kahlbaum; *d* 1·515) with stirring at room temperature. The mixture was now cooled (ice–salt), and the remainder of the acid added during 1 hour with rapid stirring, which was continued for a further 30 minutes. The separated solid (20 g.) was collected, dried in air, and crystallised from acetic acid, from which 6-nitrocholesteryl nitrate was obtained in needles, m. p. 128°. A mixture of the nitro-ester (28 g.), zinc dust (50 g.), acetic acid (400 c.c.), and water (75 c.c.) was heated on the steam-bath for 2 hours, care being taken to prevent the reaction becoming vigorous. The mixture was then heated under reflux for a further 10 hours and largely diluted with water. The product, isolated by means of ether, was hydrolysed by heating under reflux with a mixture of hydrochloric acid (85 c.c.) and alcohol (300 c.c.) for 1½ hours. The solid (16—18 g.), m. p. 136—138°, which separated on cooling was crystallised from alcohol, from which 6-ketocholestanol separated in needles, m. p. 140—141°. A solution of this (15 g.) in pyridine (30 c.c.) was treated with acetic anhydride (15 c.c.), and the mixture heated on the steam-bath for 1 hour. Water was added, the

solution cooled, and the crystalline solid (15 g.), m. p. 122—124°, collected. After one crystallisation from alcohol this gave 6-ketocholestanyl acetate in prisms, m. p. 128—129°.

5 : 7-*Dibromo-6-ketocholestanyl Acetate* (III).—(a) 6-Ketocholestanyl acetate (6·0 g.) in acetic acid (40 c.c.) was treated at 23° with 1 drop of hydrogen bromide in acetic acid (50%) and then with a solution of bromine in acetic acid (88 c.c.; 5%; 2 mols.), added during 3 minutes with shaking. The 5-bromo-6-ketocholestanyl acetate which at first separated gradually redissolved and after 75 minutes the solution was clear and the bromine absorption complete. After warming and dilution with water (20 c.c.) crystallisation was induced by scratching. The separated solid (3·4 g.) was crystallised from aqueous acetone, from which 5 : 7-*dibromo-6-ketocholestanyl acetate*, m. p. 152°, $[\alpha]_D^{20°}$ − 140° ($l$ = 1, $c$ = 0·6 in chloroform), separated in aggregates of fine needles. The dibromide was dimorphous, separating on prolonged standing from either acetic acid or acetone in magnificent rhombic crystals; the two forms were readily interconvertible (Found: C, 57·7; H, 7·3. $C_{29}H_{46}O_3Br_2$ requires C, 57·8; H, 7·7%). It reacted neither with sodium iodide in alcohol nor with *o*-phenylenediamine (cf. 2 : 4-dibromocholestanone; Ruzicka, Bosshard, and Wirz, *Helv. Chim. Acta*, 1936, **19**, 1147; Inhoffen, *Ber.*, 1937, **70**, 1695).

(b) 5-Bromo-6-ketocholestanyl acetate (500 mg.) in acetic acid (7 c.c.) was treated with bromine in acetic acid (3·5 c.c.; 5%; 1·2 mols.) and hydrogen bromide in acetic acid (0·3 c.c.; 50%). The mixture was maintained at 30° for 30 minutes, largely diluted with water, and the solid collected. Snccessive crystallisation from acetic acid and aqueous acetone gave 5 : 7-dibromo-6-ketocholestanyl acetate (200 mg.), m. p. 152°, identical with the specimen prepared by method (a).

(c) A mixture of 7-bromo-6-ketocholestanyl acetate (3·0 g.) and aliquot proportions of bromine and hydrogen bromide solutions in acetic acid was set aside at 23° for 40 hours. Subsequent procedure as described under (b) gave 5 : 7-dibromo-6-ketocholestanyl acetate (800 mg.), m. p. 152°, not depressed by admixture with an authentic specimen. Careful examination of the mother-liquors failed to yield any other homogeneous product.

5′ : 7-*Dibromo-6-ketocholestanyl Acetate* (IV).—(a) 6-Ketocholestanyl acetate (3·0 g.) in acetic acid (20 c.c.) was treated with a solution of bromine in acetic acid (22 c.c.; 5%; 1 mol.) at 23°, a drop of hydrogen bromide solution in acetic acid being added to induce reaction. The bromine addition was effected at such a rate that free bromine was not present in the solution, the addition extending over 3 minutes. The mixture was then treated with a further mol. of bromine in acetic acid, added rapidly with stirring, and set aside for 18 hours at room temperature. After warming and dilution with water, crystallisation was induced by scratching. The crude solid was recrystallised from acetic acid, from which 5′ : 7-*dibromo-6-ketocholestanyl acetate* separated in lustrous plates, m. p. 129°, $[\alpha]_D^{20°}$ − 51·1° ($l$ = 1, $c$ = 2·78 in chloroform). It was more soluble in the common organic solvents than the isomeric 5 : 7-dibromide, but less soluble than 7-bromo-6-ketocholestanyl acetate (Found: C, 57·6; H, 7·4. $C_{29}H_{46}O_3Br_2$ requires C, 57·8; H, 7·7%).

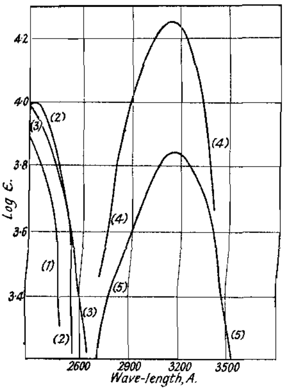
(b) A mixture of 5-bromo-6-ketocholestanyl acetate (1·0 g.), acetic acid (18 c.c.), bromine in acetic acid (6·6 c.c.; 5%; 1·1 mols.), and hydrogen bromide in acetic acid (0·3 c.c.; 50%) was heated on the steam-bath for 15 minutes, and the reaction mixture poured into water. After 12 hours, the clear solution was decanted from the hard resin, and the latter taken up in hot acetic acid. A small amount of insoluble oil was removed, and the solution cooled. The solid separating was recrystallised from acetic acid, yielding 5′ : 7-dibromo-6-ketocholestanyl acetate (100 mg.), m. p. 129°, not depressed on admixture with the specimen prepared by method (a).

*7-Bromo-6-ketocholestanyl Acetate from* 5 : 7- *and* 5′ : 7-*Dibromo-6-ketocholestanyl Acetates.*—(a) 5 : 7-Dibromo-6-ketocholestanyl acetate (700 mg.) in acetic acid (32 c.c.) was set aside at 22° for 24 hours with a solution of hydrogen bromide in acetic acid (1·25 c.c.; 50%; 2·0 mols.). The solid precipitated by dilution with water was crystallised from acetone, giving 7-bromo-6-ketocholestanyl acetate (300 mg.), m. p. 144—145°, unaltered on admixture with an authentic specimen.

(b) A solution of 5′ : 7-dibromo-6-ketocholestanyl acetate (500 mg.) in acetic acid (5 c.c.) was heated on the steam-bath for 15 minutes with a solution of hydrogen bromide in acetic acid (1·0 c.c.; 50%; 1·1 mols.), the mixture showing a play of colour, passing through green to brown. Precipitation with water gave an oil, which was isolated with ether and taken up in acetic acid. After long standing in a vacuum over potassium hydroxide, 7-bromo-6-ketocholestanyl acetate (120 mg.) separated, which, after a single recrystallisation from acetic acid, had m. p. 144—145°, unaltered on admixture with an authentic specimen.

6-*Keto*-3-*acetoxy*-$\Delta^{2:4}$-*cholestadiene* (V).—A solution of either 5 : 7- or 5′ : 7-dibromo-6-ketocholestanyl acetate (3·0 g.) in anhydrous pyridine (75 c.c.) was heated under reflux for 6½ hours. Water was added to the hot solution until it became cloudy and the solid separating on cooling (1·2 g.) was crystallised from acetic acid, from which 6-*keto*-3-*acetoxy*-$\Delta^{2:4}$-*cholestadiene* separated in pale yellow, flat needles, m. p. 139—140°, $[\alpha]_D^{20°} + 27°$ ($l = 1$, $c = 0·6$ in chloroform) (Found: C, 79·4; H, 10·1. $C_{29}H_{44}O_3$ requires C, 79·0; H, 10·0%). *Light absorption in alcohol* (figure): Maximum, 3170 A.; log ε = 3·8.

3 : 6-*Diketo*-$\Delta^4$-*cholestene* (VI).—A solution of 6-keto-3-acetoxy-$\Delta^{2:4}$-cholestadiene (100 mg.) in methyl alcohol (10 c.c.) was treated with a solution of sodium methoxide in methyl alcohol (3 c.c.; 10%), and the mixture set aside at 22° for 18 hours. The solution was acidified with dilute acetic acid, and the crude solid twice crystallised from methyl alcohol, 3 : 6-diketo-$\Delta^4$-cholestene (50 mg.) being obtained, m. p. 122—123°, unaltered on admixture with an authentic specimen.




(1) 7-*Hydroxy*-6-*keto*-3-*acetoxy*-$\Delta^4$-*cholestene* (IX).
(2) 6-*Keto*-3-*acetoxy*-7-*ethoxy*-$\Delta^4$-*cholestene* (XIV).
(3) 3-*Hydroxy*-6-*keto*-7-*ethoxy*-$\Delta^4$-*cholestene*.
(4) 6-*Keto*-7-*methoxy*-$\Delta^{2:4:7}$-*cholestatriene* (XV).
(5) 6-*Keto*-3-*acetoxy*-$\Delta^{2:4}$-*cholestadiene* (V).

7-*Hydroxy*-6-*keto*-3-*acetoxy*-$\Delta^4$-*cholestene* (IX).—The pyridine mother-liquor from 6-keto-3-acetoxy-$\Delta^{2:4}$-cholestadiene was largely diluted with water and extracted with ether. The extract was washed with dilute sulphuric acid and water, dried, and the solvent removed. Repeated crystallisation of the solid residue from acetic acid gave 7-*hydroxy*-6-*keto*-3-*acetoxy*-$\Delta^4$-*cholestene* (450 mg.), m. p. 227—229°, in flat needles sparingly soluble in alcohol and in acetic acid. This compound, which is the sole product of treatment of the 5′ : 7-dibromide with a boiling solution of silver nitrate in pyridine, fails to give a coloration with tetranitromethane in chloroform, ferric chloride in alcohol, antimony trichloride in chloroform, or with the Tortelli–Jaffé reagent (Found: C, 75·9; H, 10·0; *M*, 400 $C_{29}H_{46}O_4$ requires C, 75·9; H, 10·1%; *M*, 458). *Active hydrogen determination* (Zerewitinoff): The unsaturated ketone (6·61 mg.) evolved 0·30 c.c. of methane, measured at 30° and 763 mm., corresponding to 0·9 atom of active hydrogen per mole. *Microhydrogenation*: The unsaturated ketone (4·780 mg.), when shaken in acetic acid with palladium–barium sulphate, absorbed 0·255 c.c. of hydrogen at 20° and 753 mm., corresponding to $|\overline{_{1·1}}$. *Light absorption in alcohol* (figure): At 2280 A., log ε = 3·9. A solution of the keto-alcohol (40 mg.) in anhydrous pyridine (1·0 c.c.) and benzoyl chloride (0·5 c.c.) was heated on the steam-bath for 3 hours. The oil obtained on dilution with water and ether extraction crystallised from methyl alcohol. After three recrystallisations from ether–methyl alcohol the *monobenzoate* was obtained in glistening needles, m. p. 136—137° (Found: C, 78·7; H, 9·2. $C_{35}H_{50}O_4$ requires C, 78·6; H, 9·4%).

3 : 7-*Dihydroxy*-6-*keto*-$\Delta^4$-*cholestene*.—7-Hydroxy-6-keto-3-acetoxy-$\Delta^4$-cholestene (50 mg.) was heated under reflux with a solution of sodium methoxide in methyl alcohol (15 c.c.; 5%) for 30 minutes. The solid separating on dilution with water was thrice crystallised from aqueous methyl alcohol, giving 3 : 7-*dihydroxy*-6-*keto*-$\Delta^4$-*cholestene* in felted needles, m. p. 220—222°. The dihydroxy-ketone was very soluble in methyl alcohol, from which it separated in long flat prisms (Found: C, 78·1; H, 10·7. $C_{27}H_{44}O_3$ requires C, 77·8; H, 10·7%).

7-*Bromo*-6-*keto*-3 : 5′-*diacetoxycholestane* (XII).—A solution of 5′ : 7-dibromo-6-ketocholestanyl acetate (1·0 g.) and freshly fused potassium acetate (2·0 g.) in acetic acid (400 c.c.) was heated on the steam-bath for 1½ hours. Water (5 c.c.) was added and the solid which separated was crystallised from acetic acid, yielding 7-*bromo*-6-*keto*-3 : 5′-*diacetoxycholestane* (400 mg.) in prisms, m. p. 198° (decomp.), sparingly soluble in methyl alcohol, but moderately soluble in ether, acetone, and acetic acid (Found: C, 63·7; H, 8·2. $C_{31}H_{49}O_5Br$ requires C, 64·0; H, 8·5%).

6-*Keto*-3-*acetoxy*-7-*ethoxy*-$\Delta^4$-*cholestene* (XIV).—A solution of 5′ : 7-dibromo-6-ketocholes-

tanyl acetate (3·0 g.) in absolute alcohol (220 c.c.) was heated under reflux for 1 hour with freshly fused sodium acetate (4·5 g.). The hot solution was diluted with water until just cloudy; on cooling, 7-bromo-6-keto-3 : 5′-diacetoxycholestane (500 mg.) separated, which after three crystallisations from methyl alcohol had m. p. 198°, not depressed on admixture with an authentic specimen. The original mother-liquor was gradually diluted with water, whereby a small quantity of oil separated. Further dilution of the decanted solution gave a solid (600 mg.), m. p. 100—103°, slow crystallisation of which from methyl alcohol gave a mixture of small hard nodules and large plates. The mixture was separated mechanically, recrystallisation of the nodules from methyl alcohol giving a further quantity of 7-bromo-6-keto-3 : 5′-diacetoxycholestane. The large plates were thrice recrystallised from alcohol; *6-keto-3-acetoxy-7-ethoxy-Δ⁴-cholestane* (300 mg.) was then obtained, m. p. 119—120°. With tetranitromethane in chloroform the ether gave a yellow coloration; it sublimed unchanged at 140°/$10^{-3}$ mm. (Found : C, 76·5; H, 10·4; OEt, 8·4. $C_{31}H_{50}O_4$ requires C, 76·5; H, 10·4; OEt, 9·2%). *Light absorption in alcohol* (figure) : At 2300 A., log ε = 3·9.

6 : 7-*Diketocholestanyl Acetate from* 5′ : 7-*Dibromo-6-ketocholestanyl Acetate*.—The mother-liquor obtained after the removal of the solid, m. p. 100—103° (above), was again gradually diluted with water. A further quantity of the ether, m. p. 119—120°, was obtained and subsequently a solid, m. p. 110—128°, which gave an intense green-violet coloration with alcoholic ferric chloride solution. After two crystallisations from aqueous acetone the latter gave 6 : 7-diketocholestanyl acetate (100 mg.), m. p. 156—157°, which showed no depression on admixture with an authentic specimen and was characterised by the formation of the quinoxaline derivative, m. p. 186—187°.

6-*Keto*-3 : 5′-*diacetoxycholestane* (XIII).—A solution of 7-bromo-6-keto-3 : 5′-diacetoxy-cholestane (70 mg.) in ether (70 c.c.) was treated at 20° with aluminium amalgam (2 g.), water being periodically added to the reaction mixture during 3 hours. After filtration and removal of solvent the product (40 mg.), which readily solidified on grinding with methyl alcohol, was twice crystallised from the same solvent, 6-keto-3 : 5′-diacetoxycholestane separating in long hard needles, m. p. 169—170°, not depressed when mixed with an authentic specimen (Found : C, 74·2; H, 10·2. Calc. for $C_{31}H_{50}O_5$ : C, 74·0; H, 10·0%).

3-*Hydroxy-6-keto-7-ethoxy-Δ⁴-cholestene*.—6-Keto-3-acetoxy-7-ethoxy-Δ⁴-cholestene (50 mg.) in methyl alcohol (5 c.c.) was heated under reflux for 30 minutes with a solution of sodium methoxide in methyl alcohol (5 c.c.; 10%). The crude material separating on dilution with water was thrice crystallised from aqueous methyl alcohol, from which *3-hydroxy-6-keto-7-ethoxy-Δ⁴-cholestene* separated in hair-like needles, m. p. 113° (Found : C, 78·5; H, 10·8. $C_{29}H_{48}O_3$ requires C, 78·3; H, 10·9%). *Light absorption in alcohol* (figure) : At 2300 A., log ε = 4·0.

6-*Keto-7-methoxy-Δ*$^{2:4:7}$*-cholestatriene* (XV).—A solution of 5′ : 7-dibromo-6-ketocholestanyl acetate (1·6 g.) in dry *n*-butyl alcohol (80 c.c.) was heated under reflux for 7 hours with freshly fused potassium acetate (3·0 g.). The product, isolated by means of ether, gave an intense coloration with alcoholic ferric chloride. Crystallisation was effected from methyl alcohol containing a little acetone, and recrystallisation from ether–methyl alcohol yielded clusters of needles, m. p. 116—118°, still giving an intense red coloration with ferric chloride. Two further crystallisations from methyl alcohol gave *6-keto-7-methoxy-Δ*$^{2:4:7}$*-cholestatriene* in fine needles, m. p. 119—121°, which did not give a ferric chloride coloration (Found : C, 81·9; H, 10·7. $C_{28}H_{42}O_2$ requires C, 81·9; H, 10·3%). *Light absorption in alcohol* (figure) : Maximum, 3150 A.; log ε = 4·2.

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# 24. *Union of Aryl Nuclei. Part I. Some Extensions of the Gomberg Reaction.*

By W. S. M. Grieve and D. H. Hey.

Methods for synthesising biaryl compounds by means of reactions involving diazo-compounds are reviewed with special reference to the union of two dissimilar aryl nuclei. Attempts to increase the yields obtained in the reaction, developed by Gomberg and his co-workers (*J. Amer. Chem. Soc.*, 1924, **46**, 2339; 1926, **48**, 1372), between a diazotised base and a neutral aromatic liquid in the presence of aqueous alkali, $Ph{\cdot}N_2{\cdot}OH + PhR \longrightarrow Ph{\cdot}C_6H_4R + N_2 + H_2O$, are unsuccessful. The scope of the reaction is extended to include the use of (a) solid reactants in solution and (b) bases of the naphthalene series; *e.g.*, methyl anthranilate and naphthalene, aniline and diphenyl, *p*-nitroaniline and diphenyl, and *p*-anisidine and benzophenone give *methyl o-α-naphthylbenzoate*, *p*-diphenylbenzene, 4′-nitro-*p*-diphenylbenzene, and 4-methoxy-4′-benzoyldiphenyl respectively. The solvent, which is either chloroform or carbon tetrachloride, is not entirely inert. When diazotised aniline is used with carbon tetrachloride, for example, an appreciable quantity of chlorobenzene is formed. This observation is of particular interest in correlating the mechanism of the Gomberg reaction with that of the related reactions of nitrosoacetanilide, phenylazotriphenylmethane, and dibenzoyl peroxide, which is regarded as non-ionic in type. Experimental evidence is also included to show that the two-phase system is an essential feature of the Gomberg reaction, an observation which is in agreement with the representation of the reaction as a non-ionic process. Reactions carried out between diazotised α- and β-naphthylamine and benzene give α- and β-phenylnaphthalene respectively, but in small yield.

Several methods are available for the preparation of biaryl compounds through the agency of diazonium compounds; *e.g.*, Vorländer and Meyer (*Annalen*, 1902, **320**, 122) prepared a number of symmetrical diphenyl derivatives from aromatic diazonium salts in the presence of ammoniacal cuprous oxide, a reaction which has achieved industrial importance in its application to α-naphthylamine-8-carboxylic acid (I.G., E.P. 278,100). In many cases, however, the reaction follows a different course and gives rise to azo-compounds. Examples of the preparation of symmetrical biaryls from diazonium compounds through the agency of metallic copper (Gattermann, *Ber.*, 1890, **23**, 1226; Knoevenagel, *Ber.*, 1895, 28, 2049; Ullmann, *Ber.*, 1896, **29**, 1878; Niementowski, *Ber.*, 1901, **34**, 3325; Gerngross and Dunkel, *Ber.*, 1924, **57**, 739; Gerngross, Schachnow, and Jonas, *ibid.*, p. 747) and cuprous chloride (Ullmann and Forgan, *Ber.*, 1901, **34**, 3802; Ullmann and Frentzel, *Ber.*, 1905, **38**, 726) have been recorded, and numerous other agents have also been employed (Griess, *Annalen*, 1866, **137**, 79; Oddo, *Gazzetta*, 1890, **20**, 663; Beeson, *Amer. Chem. J.*, 1894, **16**, 235; Culmann and Gasiorowski, *J. pr. Chem.*, 1889, **40**, 97). The synthesis of unsymmetrical biaryls has also been effected by means of reactions involving diazonium compounds (Hirsch, *Ber.*, 1890, **23**, 3705; 1892, **25**, 1973; Norris, Macintyre, and Corse, *Amer. Chem. J.*, 1903, **29**, 120; Oddo and Curatolo, *Gazzetta*, 1895, **25**, 126; Möhlau and Berger, *Ber.*, 1893, **26**, 1196, 1994; Kühling, *Ber.*, 1895, **28**, 41, 523; 1896, 29, 165; Bamberger, *Ber.*, 1895, **28**, 403; 1896, **29**, 446; Chatterjee, *J. Indian Chem. Soc.*, 1935, **12**, 410, 690). Some of these methods involve the isolation of dry, or semi-dry, unstable and often explosive intermediates, and in order to overcome this disadvantage Gomberg and Bachmann (*J. Amer. Chem. Soc.*, 1924, **46**, 2339) introduced a procedure which eliminates the necessity of isolating the solid diazo-compound from its aqueous solution. Its use was extended by Gomberg and Pernert (*J. Amer. Chem. Soc.*, 1926, **48**, 1372). In its simplest form this reaction, which forms the basis of the experimental work in this communication, may be represented thus: $Ph{\cdot}N_2{\cdot}OH + PhR \longrightarrow$ *o*- and *p*-$Ph{\cdot}C_6H_4R + N_2 + H_2O$. Further examples of its use have been described by Grieve and Hey (J., 1932, 1888, 2245; 1934, 1797), Hey (J., 1932, 2636), and Cook and Cook (*J. Amer. Chem. Soc.*, 1933, **55**, 1212).

One of the chief characteristics of the reaction is the fact that it gives rise to " ampho-

teric" or ***invariable ortho-para substitution*** (Grieve and Hey, J., 1934, 1797), *i.e.*, the phenyl or substituted phenyl group always enters the aromatic nucleus of the second component $C_6H_5R$ at the ortho- and/or para-positions with regard to R, irrespective of the usual directive influence of R with reference to the normal substitution reactions by a kationoid or anionoid reagent. This unusual phenomenon, already noted by Kühling (*loc. cit.*) and Gomberg and Pernert (*loc. cit.*, p. 1379), has been encountered in two other reactions as well as possibly in a third (Hey, J., 1934, 1966), and these additional reactions may therefore be cited as further examples of methods for the preparation of unsymmetrical biaryls. For example, the reaction between nitrosoacylarylamines and an aromatic component (Bamberger, *Ber.*, 1897, **30**, 366; Kliegl and Huber, *Ber.*, 1920, **53**, 1655; Hey, J., 1932, 2636; Grieve and Hey, J., 1934, 1797), *viz.*, $Ar\cdot N(NO)\cdot COR + C_6H_5R' \longrightarrow$ *o*/*p*-$Ar\cdot C_6H_4R' + N_2 + R\cdot CO_2H$, and also that between a diaroyl peroxide and an aromatic component (Gelissen and Hermans, *Ber.*, 1925, **28**, 285, 476; Hey, J., 1934, 1966; Wieland, Schapiro, and Metzger, *Annalen*, 1934, **513**, 93), *viz.*, $Ar\cdot CO\cdot O\cdot O\cdot COAr + C_6H_5R \longrightarrow$ *o*/*p*$Ar\cdot C_6H_4R + CO_2 + Ar\cdot CO_2H$, may, in selected cases, be of great value in this respect.

Further developments in the methods available for the preparation of unsymmetrical biaryls are obviously desirable and the present communication deals mainly with possible extensions of the Gomberg reaction to include the use of (a) reacting components which are solid at the temperature of the reaction ($< 20°$) and (b) bases of the naphthalene series.

Attempts have also been made to increase the yields by variations in experimental conditions, diazotised aniline and benzene being used, as the ease with which the product (diphenyl) can be isolated enables reliable estimations of yield to be readily obtained. Two methods of procedure are possible: either the diazotised base is added to a cold well-stirred mixture of the second component (which is a neutral aromatic liquid immiscible with water) and sufficient aqueous sodium hydroxide to ensure the mixture being alkaline on the completion of the addition, or the appropriate quantity of aqueous sodium hydroxide is added to the mixture of the aqueous diazonium solution and the second component. The former method is recommended by Gomberg and Pernert (*loc. cit.*) for aniline and the toluidines, and the latter for halogeno- and nitro-anilines. In our experience there is, in most cases, little to choose between the two. By the second method reactions were carried out (a) in presence of magnesium sulphate (cf. Gomberg and Bachmann, *J. Amer. Chem. Soc.*, 1927, **49**, 250), (b) in presence of copper sulphate, (c) with addition of aqueous ammonia in place of sodium hydroxide, (d) in an atmosphere of nitrogen, solntions saturated with nitrogen being used, (e) with addition of aqueous sodium acetate in place of sodium hydroxide, and (f) in presence of formaldehyde. By the first method reactions were carried out (a) with calcium hydroxide in place of sodium hydroxide, (b) with the addition of lissapol A as an emulsifying agent, (c) at 30° throughout the reaction, and (d) at 50° throughout the reaction. The yield of diphenyl was in no case markedly in excess of that obtained in the usual manner described by Gomberg. In the example studied, however, the reaction proceeded equally well at 30° and artificial cooling is therefore not necessary. At this temperature it is, of course, essential to use the first method of procedure; this modification may be of use with components which would solidify at lower temperatures.

In a discussion of the mechanism of this reaction Gomberg and Pernert (*loc. cit.*) conclude that "the success of the reaction is seen at once to lie in the ability of the non-aqueous liquid to extract from the aqueous layer the reactive diazo-compound as fast as it is formed." The present authors are in entire agreement with this statement, which implies that the essential reaction takes place in the non-aqueous medium and is probably non-ionic in character. In confirmation of this view it is now shown that no biaryl formation could be detected when (a) diazotised aniline and aqueous sodium benzoate, (b) diazotised anthranilic acid and aqueous sodium benzoate, or (c) diazotised anthranilic acid and benzene were used as components in the reaction. On the other hand the reaction proceeds in the normal manner when methyl benzoate is used in place of sodium benzoate in reaction (a) (Gomberg and Bachmann, *J. Amer. Chem. Soc.*, 1924, **46**, 2343), or when diazotised methyl anthranilate is used in place of anthranilic acid in reaction (c). The two-phase system thus appears to be an essential feature of the reaction, the success of which is dependent upon a favourable partition coefficient.

No experimental work has been reported previously in which the Gomberg reaction has been applied to solid reactants in solution, and the value of the reaction would be considerably enhanced if an extension in this direction could be made. The choice of a suitable solvent is limited, since it must be neutral, immiscible with water, and inert towards the highly reactive diazo-compound. In addition it should possess high solvent power and a reasonably low boiling point. It was impossible to find a solvent entirely inert, but some success attended the use of chloroform and carbon tetrachloride, although in both cases (especially the latter) some reaction with the solvent was evident and the yield of biaryl was, in general, low. The low volatility of the solid reactant, which must be present in excess, unfortunately often adds to the practical difficulty of isolating the desired product.

It was found that from diazotised methyl anthranilate and a solution of naphthalene in carbon tetrachloride, by the use of the normal procedure of Gomberg, *methyl* o-*α-naphthylbenzoate* was obtained. The free acid, obtained on hydrolysis, was converted by ring closure into *meso*benzanthrone, both by the action of aluminium chloride on the acid chloride (cf. Schaarschmidt and Georgeacopol, *Ber.*, 1918, **51**, 1082) and by the action of concentrated sulphuric acid. Further examples of the application of the Gomberg reaction to solutions of solid reactants have been provided by reactions between (a) diazotised aniline and a solution of diphenyl in chloroform and in carbon tetrachloride, which gave rise to *p*-diphenylbenzene, (b) diazotised *p*-nitroaniline and a solution of diphenyl in chloroform, which yielded 4′-nitro-*p*-diphenylbenzene, and (c) diazotised *p*-anisidine and a solution of benzophenone in carbon tetrachloride. In the last reaction 4-methoxy-4′-benzoyldiphenyl was formed, which was identical with the product resulting from the action of benzoyl chloride on 4-methoxydiphenyl in the presence of aluminium chloride, the constitution of which has been proved by an unambiguous synthesis (Hey and Jackson, J., 1936, 802).

When carbon tetrachloride was used as solvent, a considerable quantity of chlorobenzene was found in the product from reactions using diazotised aniline. This observation is of particular significance in correlating the Gomberg reaction with other reactions which give rise to biaryl formation and which, it is held, also proceed most probably by a non-ionic mechanism involving free radicals. It has been shown by Waters (J., 1937, 113) that chlorobenzene is formed when nitrosoacetanilide is dissolved in carbon tetrachloride or chloroform. Wieland and his co-workers (*Annalen*, 1934, **514**, 145) have also shown that, when phenylazotriphenylmethane is heated in carbon tetrachloride solution, chlorobenzene is formed, and a similar result was observed by Böeseken and Gelissen (*Rec. trav. chim.*, 1924, **43**, 869) in the decomposition of dibenzoyl peroxide in carbon tetrachloride. These observations, coupled with evidence from invariable ortho-para aromatic substitution, point to a similar mechanism common to all four reactions and, as indicated elsewhere (Grieve and Hey, J., 1934, 1797; Hey, *ibid.*, p. 1966; Waters, *loc. cit.*), all the available evidence is consistent with a mechanism involving the formation and transient existence of free radicals. If such is the case, only very limited success would be expected to attend the application of the Gomberg reaction to solid reactants in solution, since the highly reactive radicals would also react in large measure with the solvent molecules. The evidence contained in the present communication is entirely in agreement with these conclusions.

Hitherto bases of the naphthalene series have not been used in the Gomberg reaction. Reactions have now been carried out with both diazotised α-naphthylamine and diazotised β-naphthylamine and benzene; α- and β-phenylnaphthalene respectively were obtained, but the yields were small.

## Experimental.

*Experimental Conditions.*—The following reactions were carried out with the object of improving the yield of diphenyl obtainable from diazotised aniline and benzene, one or other of the two general methods of procedure described by Gomberg and Pernert (*loc. cit.*) being used.

(i) Aniline (31 g.), dissolved in hydrochloric acid (*d* 1·16, 83 c.c.), was diazotised at 5° with a concentrated aqueous solution of sodium nitrite. The resulting solution was added to benzene (300 c.c.) and to this mixture, vigorously stirred at 0—5°, was added gradually a solution of

sodium hydroxide (32 g.) in water (100 c.c.). Stirring was continued for 8 hours while the temperature was raised slowly to 30—35°. The benzene layer was then separated, washed with dilute hydrochloric acid and with water, dried, and distilled. The crude diphenyl was collected under reduced pressure and redistilled at atmospheric pressure. Weight, 12·5 g.; yield, 24%, calculated on the weight of aniline used. Unless otherwise stated, this method of working up the product was used in all subsequent experiments.

(ii) This reaction was carried out as in (i) except that a solution of magnesium sulphate (35 g. of the heptahydrate) in water (100 c.c.) was added to the mixture of the diazonium solution and the benzene before the addition of the alkali. Weight of diphenyl, 12·5 g.; yield, 24% (cf. Gomberg and Bachmann, *J. Amer. Chem. Soc.*, 1927, **49**, 250).

(iii) This reaction was carried out as in (ii), but larger quantities were used (47 g. of aniline) and a solution of copper sulphate (50 g. of the pentahydrate) in water (200 c.c.) was added in place of the aqueous magnesium sulphate. Weight of diphenyl, 12 g.; yield, 16%.

(iv) Aqueous ammonia (*d* 0·880, 70 c.c.) was added gradually to a stirred mixture of benzene (350 c.c.) and the diazonium solution, prepared from aniline (47 g.), kept at 0—5°. The temperature was raised gradually to 40° during 12 hours. Weight of diphenyl, 7 g.; yield, 10%.

(v) This reaction was carried out in an atmosphere of nitrogen, solutions previously saturated with this gas being used. The experimental procedure was as in (i), the quantities used being based on 47 g. of aniline. Weight of diphenyl, 17·5 g.; yield, 23%.

(vi) Aqueous sodium acetate (165 g. of the trihydrate in 400 c.c. of water) was added gradually to a cold stirred mixture of the diazonium solution, from 47 g. of aniline, and benzene (350 c.c.). Weight of diphenyl, 4 g.; yield, 5%.

(vii) This reaction was carried out as in (i), quantities based on 47 g. of aniline being used, with the addition of formaldehyde (25 c.c. of 40% solution) prior to the addition of alkali. Since difficulty was experienced in separating the two layers at the end of the reaction, the diphenyl was isolated by prolonged distillation with steam. Weight of diphenyl, 7 g.; yield, 10%.

(viii) A solution of benzenediazonium chloride, prepared from 47 g. of aniline, was added gradually to a stirred mixture of benzene (350 c.c.) and a sludge of slaked lime (46 g.) in water (200 c.c.) at 0—5°. Stirring was continued for 9 hours while the temperature was raised slowly to 40°. The mixture was acidified, and the benzene layer separated and treated as described above. Weight of diphenyl, 17·5 g.; yield, 23%.

(ix) The diazonium solution, prepared from 47 g. of aniline, was added gradually to a stirred mixture of benzene (300 c.c.) and aqueous sodium hydroxide (50 g. in 150 c.c.) with the addition of lissapol A (2 g.). Stirring was continued for 12 hours and the temperature was raised gradually from 5° to about 40°. The diphenyl was distilled in steam. Weight, 17·5 g.; yield, 23%.

(x) This reaction was carried out as in (ix), but no lissapol A was added and the temperature was maintained at 30° throughout the reaction. The diphenyl was distilled in steam. Weight, 20 g.; yield, 26%.

(xi) This reaction was carried out as in (x), but at 50°. Weight of diphenyl, 15 g.; yield, 19%.

The following reactions were carried out to find if the two-phase system of two immiscible liquids is essential.

(xii) An aqueous solution of diazotised aniline was added gradually to an aqueous solution of sodium benzoate at 5° containing a sufficient excess of alkali to neutralise the diazo-solution. No diphenylcarboxylic acid could be detected in the product.

(xiii) An aqueous solution of diazotised anthranilic acid was used in place of the diazotised aniline in reaction (xii). No diphenyldicarboxylic acid was detected.

(xiv) An aqueous solution of diazotised anthranilic acid was added to benzene, and to the resulting mixture aqueous alkali was added, under the conditions described in (i). No diphenylcarboxylic acid was detected.

(xv) A fine suspension of methyl anthranilate (50 g.) in hydrochloric acid (*d* 1·16, 83 c.c.) and water (35 c.c.) was diazotised in the normal manner and added to benzene (350 c.c.). Aqueous sodium hydroxide (27 g. in 100 c.c.) was added gradually to the stirred mixture at 0—5°. Stirring was continued for 12 hours and the temperature was raised gradually to about 30°. The benzene layer was separated, washed with concentrated hydrochloric acid and with water, and distilled. After removal of the benzene the pressure was reduced to 30 mm. and crude methyl diphenyl-2-carboxylate was collected at 190—195°. Redistillation gave the pure ester (17 g.; b. p. 307—308°/740 mm.), which on hydrolysis gave diphenyl-2-carboxylic acid, m. p. and mixed m. p. 110° (Fittig and Ostermayer, *Annalen*, 1873, **166**, 374; Graebe and Rateanu, *Annalen*, 1894, **279**, 260). Treatment with concentrated sulphuric acid at 50° gave

fluorenone, m. p. 83° after crystallisation from alcohol (Graebe and Aubin, *Ber.*, 1887, **20**, 847; Weger and Döring, *Ber.*, 1903, **36**, 881).

*The Use of Solid Reactants in Solution.—Diazotised methyl anthranilate and naphthalene.* A paste of methyl anthranilate (50 g.) in dilute hydrochloric acid (84 c.c. of acid, *d* 1·16, and 40 c.c. of water) was diazotised with aqueous sodium nitrite in the normal manner. Aqueous sodium hydroxide (27 g. in 100 c.c.) was added gradually to a vigorously stirred mixture of the diazonium solution and a solution of naphthalene (100 g.) in carbon tetrachloride (350 c.c.) at 0—5°. Stirring was continued for 10 hours and the temperature of the mixture was raised slowly to 40°. The carbon tetrachloride layer was separated, washed with water, dried, and distilled. After carbon tetrachloride and the excess of naphthalene had been collected, a small intermediate liquid fraction (b. p. 230—250°) was obtained, which consisted of methyl o-chlorobenzoate, and finally a fraction, b. p. 300—320°, which solidified when cold. Recrystallisation from methyl alcohol and then from light petroleum (b. p. 80—100°) gave *methyl* o-α-*naphthylbenzoate* in prisms, m. p. 87—88° (Found: C, 82·2; H, 5·1. $C_{18}H_{14}O_2$ requires C, 82·4; H, 5·3%). Hydrolysis of the ester with alcoholic potassium hydroxide yielded *o*-α-naphthylbenzoic acid, m. p. 159—160° (cf. Schaarschmidt and Georgeacopol, *loc. cit.*, p. 1085).

A portion of the acid (0·8 g.), suspended in benzene with the addition of phosphorus pentachloride (0·7 g.), was boiled under reflux for ½ hour; aluminium chloride (2 g.) was then added, and the mixture again boiled until evolution of hydrogen chloride had ceased. The product was poured on ice and distilled with steam to remove benzene. The residual yellowish-brown solid was washed with dilute acid and with alkali. Recrystallisation from acetic acid gave *meso*benzanthrone, m. p. 170°, both alone and on admixture with an authentic specimen.

Ring closure of the acid was also effected by keeping it at room temperature in solution in concentrated sulphuric acid containing 10% of boric acid during several days, the benzanthrone being isolated in the normal manner.

*Diazotised aniline and diphenyl.* Aqueous sodium hydroxide (100 g. in 250 c.c.) was added slowly to an ice-cold stirred mixture of an aqueous solution of benzenediazonium chloride, prepared from 93 g. of aniline (1 mol.), and a solution of diphenyl (200 g.) in chloroform (600 c.c.). Stirring was continued for 10 hours and the temperature was raised slowly to 40°. The chloroform layer was separated, washed with water, dried, and distilled. The greater part of the excess of diphenyl was collected at atmospheric pressure, but the pressure was reduced to remove the last traces. *p*-Diphenylbenzene, m. p. 206—208°, was extracted from the non-volatile residue by means of a hot mixture of benzene and light petroleum (b. p. 80—100°) (cf. Schultz, *Annalen*, 1874, **174**, 230). In a similar reaction using carbon tetrachloride in place of chloroform, an appreciable quantity of chlorobenzene (16 g.) was collected during the distillation. In a reaction using diazotised aniline, aqueous sodium hydroxide, and carbon tetrachloride alone without any solute, carried out as above, 12 g. of chlorobenzene were obtained from 46·5 g. of aniline.

*Diazotised* p-*nitroaniline and diphenyl* (with J. L. Dunn). When diazotised *p*-nitroaniline, prepared from 46 g. of *p*-nitroaniline (⅓ mol.), was used in place of diazotised aniline in the previous reaction, 4′-nitro-*p*-diphenylbenzene * was obtained, which was extracted from the non-volatile residue with hot glacial acetic acid. Crystallisation from glacial acetic acid gave golden-yellow needles, m. p. 214—215° (Found: C, 78·2; H, 4·7; N, 5·2. Calc. for $C_{18}H_{13}O_2N$: C, 78·5; H, 4·7; N, 5·1%). On reduction with iron filings and hydrochloric acid in the usual manner, 4′-amino-*p*-diphenylbenzene, m. p. 196—198°, was obtained (cf. Pummerer, Binapfl, Bittner, and Schuegraf, *Ber.*, 1922, **55**, 3095; Pummerer and Bittner, *Ber.*, 1924, **57**, 84).

*Diazotised* p-*anisidine and benzophenone* (with E. R. B. Jackson). A solution of *p*-anisidine (50 g.) in hydrochloric acid (*d* 1·16, 100 c.c.) was diazotised with sodium nitrite (28·5 g.) in the normal manner at 0° and added to an ice-cold solution of benzophenone (200 g.) in carbon tetrachloride (350 c.c.). Aqueous sodium hydroxide (30 g. in 100 c.c.) was added to the vigorously stirred, cold mixture during 2 hours. Stirring was continued until the temperature reached that of the room. After standing overnight, the carbon tetrachloride layer was separated, washed with water, and distilled. After removal of the excess of benzophenone under reduced pressure (25 mm.), a viscous oil (3 g.) distilled at 280—285°, which solidified when cold. After crystallisation from benzene–alcohol 4-methoxy-4′-benzoyldiphenyl was obtained in almost colourless leaflets, m. p. 166° alone and in admixture with an authentic specimen (Hey and Jackson, *loc. cit.*) (Found: C, 83·0; H, 6·0. Calc. for $C_{20}H_{16}O_2$: C, 83·3; H, 5·6%).

* Since the completion of this work 4′-nitro-*p*-diphenylbenzene has been obtained by Basford (J., 1937, 1442) by another method.

*Experiments with α- and β-Naphthylamine.—Diazotised α-naphthylamine and benzene.* A suspension of α-naphthylamine (72 g.) in hydrochloric acid (*d* 1·16, 125 c.c.) and water (50 c.c.) was diazotised in the normal manner and added to benzene (400 c.c.). To the mixture, aqueous sodium hydroxide (50 g. in 200 c.c.) was added gradually, with stirring, at 0—5°. After 10 hours with a gradual rise in temperature to 40°, the benzene was removed with steam and the dark solid residue was heated with tin and hydrochloric acid to remove azo-compounds. The insoluble residue was extracted several times with hot benzene. Distillation of the benzene extract yielded α-phenylnaphthalene as a yellow oil, b. p. 320—330°, in small yield. Oxidation with potassium permanganate gave *o*-benzoylbenzoic acid, m. p. 93°, or 125° after dehydration (cf. Möhlau and Berger, *Ber.*, 1893, **26**, 1199).

*Diazotised β-naphthylamine and benzene.* This reaction was carried out exactly as described above for α-naphthylamine, but half the quantities were used. The residue (41 g.) obtained after steam-distillation was extracted repeatedly with light petroleum (b. p. 80—100°). Evaporation of the extracts deposited β-phenylnaphthalene (4 g.) as a slightly pink, crystalline solid. Recrystallisation from alcohol gave pearl-like flakes, m. p. 100—101° alone and in admixture with an authentic specimen kindly supplied by Dr. F. S. Spring (cf. J., 1934, 1332).

In both reactions with the naphthylamines a considerable quantity of dark insoluble granular material was formed.

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## 25. *Union of Aryl Nuclei. Part II. Chloro-, Bromo-, and Nitro-fluorenones.*

By I. M. Heilbron, D. H. Hey, and R. Wilkinson.

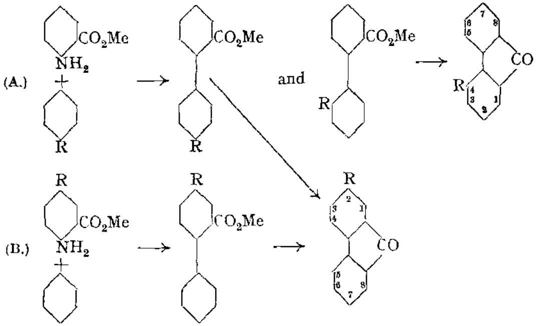
By means of the reaction due to Gomberg and his collaborators (*J. Amer. Chem. Soc.*, 1924, **46**, 2339; 1926, **48**, 1372), diazotised methyl anthranilate (or a derivative) and a neutral aromatic liquid being used, nuclear-substituted diphenyl-2-carboxylic acids become readily available, from which the corresponding substituted fluorenones may be obtained quantitatively on ring closure. Various alternative methods of procedure which present themselves are investigated.

It has long been known that derivatives of fluorenone may be prepared either by direct substitution or by substitution in fluorene, followed by oxidation. If the substituting agent is kationoid in type, the substituent atom or group first enters the 2-position, and then position 7 and to a smaller extent position 5. The scope of both these methods is thus limited. Moreover, when these methods are used, mixtures of mono- and di-substitution products, often contaminated with unsubstituted material, are frequently encountered, from which it is difficult to separate pure products (Courtot and Vignati, *Bull. Soc. chim.*, 1927, **41**, 58; *Compt. rend.*, 1927, **184**, 1179; Korczynski, Karlowska, and Kierzek, *Bull. Soc. chim.*, 1927, **41**, 65; Thurston and Shriner, *J. Amer. Chem. Soc.*, 1935, **57**, 2164). Alternative methods for the preparation of substituted fluorenones have been reviewed recently by Miller and Bachman (*J. Amer. Chem. Soc.*, 1935, **57**, 2443).

It has been shown (preceding paper) that by means of the procedure due to Gomberg and his co-workers (*J. Amer. Chem. Soc.*, 1924, **46**, 2339; 1926, **48**, 1372) it is possible to obtain diphenyl-2-carboxylic acid (or its methyl ester) from diazotised methyl anthranilate and benzene in the presence of alkali. This reaction is now utilised to provide chloro-, bromo-, and nitro-diphenyl-2-carboxylic acids, from which the corresponding substituted fluorenones are derived by ring closure—a long-known method of preparing fluorenones (Fittig and Ostermayer, *Annalen*, 1873, **166**, 376; Graebe and Aubin, *Ber.*, 1887, **20**, 845; Weger and Döring, *Ber.*, 1903, **36**, 881).

By means of this method monosubstituted derivatives of diphenyl-2-carboxylic acid

may be obtained either from diazotised methyl anthranilate and a monosubstituted benzene derivative (A), or from the diazotised methyl ester of a monosubstituted anthranilic acid and benzene (B).




In the former process a mixture of diphenyl-2-carboxylic esters results, as indicated above, where R may be either a so-called ortho-para-directing or meta-directing group or atom (cf. Grieve and Hey, J., 1934, 1797), from which two fluorenones are obtained on ring closure. The latter procedure gives a single product and is therefore preferred.

From the reactions between diazotised methyl 4-chloro- and 4-bromo-anthranilate and benzene, 5-*chloro-* and 5-*bromo-diphenyl*-2-*carboxylic acids* were obtained, which were converted quantitatively by ring closure with concentrated sulphuric acid at 50° into 3-*chlorofluorenone* and 3-bromofluorenone respectively. Similarly, diazotised methyl 5-chloro- and 5-bromo-anthranilate and benzene yielded 4-*chlorodiphenyl*-2-*carboxylic acid* and the 4-bromo-analogue, from which 2-chloro- and 2-bromo-fluorenone respectively were obtained. Further, from the reaction between the diazotised methyl ester of 5-nitroanthranilic acid and benzene, 4-*nitrodiphenyl*-2-*carboxylic acid* was obtained; this was converted into 2-nitrofluorenone. On the other hand, no product could be isolated from the reaction between diazotised methyl anthranilate and nitrobenzene. The reaction between diazotised methyl anthranilate and either chloro- or bromo-benzene gave mixtures of probably 2′- and 4′-halogenodiphenyl-2-carboxylic acids; these yielded mixtures of the 4- and 2-halogenofluorenones, which could not be separated completely (cf. Miller and Bachman, *loc. cit.*). The combined yields of the mixed acids resulting from these reactions (method A) were less satisfactory than the yields of the single acids resulting from the reactions using a substituted methyl anthranilate and benzene (method B).

The 2-chlorofluorenone obtained from 4-chlorodiphenyl-2-carboxylic acid was identical with a specimen obtained from the ring closure of 4′-*chlorodiphenyl*-2-*carboxylic acid*, which was prepared from 4′-*chloro*-2-*methyldiphenyl* by oxidation. The latter was obtained from the reaction between diazotised *p*-chloroaniline and toluene, which yielded some 4′-chloro-4-methyldiphenyl but mainly 4′-chloro-2-methyldiphenyl. A similar result was recorded by Gomberg and Pernert (*J. Amer. Chem. Soc.*, 1926, **48**, 1378) for the reaction between diazotised *p*-bromoaniline and toluene.

## EXPERIMENTAL.

*Preparation of Substituted Anthranilic Esters.*—Methyl 5-chloroanthranilate was prepared by the direct chlorination of methyl anthranilate (Freundler, *Bull. Soc. chim.*, 1911, **9**, 605). Methyl 5-bromoanthranilate was obtained by bromination of methyl trichloroethylidene-anthranilate, as recommended by Freundler (*loc. cit.*; cf. Wheeler, *J. Amer. Chem. Soc.*, 1909,

31, 565). The 4-halogenoanthranilic esters were prepared by the following sequence of reactions: 2-nitro-*p*-toluidine ⟶ 4-halogeno-2-nitrotoluene ⟶ 4-halogeno-*o*-toluidine ⟶ 4-halogenoaceto-*o*-toluidide ⟶ 4-halogeno-2-acetamidobenzoic acid ⟶ methyl 4-halogeno-2-aminobenzoate (cf. Friedländer, Bruckner, and Deutsch, *Annalen*, 1912, **388**, 23; Cohn, *Monatsh.*, 1901, **22**, 473; Robertson and Waters, J., 1931, 72; Frejka and Vymetal, *Coll. Czech. Chem. Comm.*, 1935, **7**, 436). The reduction of the nitro-group was effected with stannous chloride, and the oxidation of the methyl group with neutral potassium permanganate. Methyl 5-nitroanthranilate was prepared by nitration of acetylanthranilic acid, followed by hydrolysis and esterification (cf. Rupe, *Ber.*, 1897, **30**, 1097; Baly, Tuck, and Marsden, J., 1910, **97**, 1502; Bogert and Scatchard, *J. Amer. Chem. Soc.*, 1919, **41**, 2065).

*3-Chlorofluorenone.*—A paste of methyl 4-chloroanthranilate (18·5 g., 0·1 mol.), hydrochloric acid (30 c.c., *d* 1·16), and water (10 c.c.) was diazotised in the normal manner with aqueous sodium nitrite. Aqueous sodium hydroxide (9 g. in 30 c.c.) was gradually added to a vigorously stirred mixture of the ice-cold diazonium solution and benzene (150 c.c.). Stirring was continued for 10 hours while the temperature was raised to 25°. The benzene layer was separated, washed with concentrated hydrochloric acid and with water, dried, and distilled. After removal of the excess of benzene the crude 5-chlorodiphenyl-2-carboxylic ester was collected under reduced pressure (b. p. 180—190°/20 mm.; yield 25%, calculated on weight of methyl 4-chloroanthranilate). The crude ester was boiled under reflux for 4 hours with 20% aqueous sodium hydroxide, and the solution diluted with water, filtered, and acidified. The precipitated *5-chlorodiphenyl-2-carboxylic acid* crystallised from dilute alcohol in needles, m. p. 152° (Found: C, 67·1; H, 4·3. $C_{13}H_9O_2Cl$ requires C, 67·1; H, 3·9%).

The acid (or ester) was warmed to 50° with ten times its weight of concentrated sulphuric acid and kept at that temperature for 10 minutes. When the solution was poured into water, *3-chlorofluorenone* separated as a yellow precipitate, which after crystallisation from alcohol melted at 157° (Found: C, 72·8; H, 3·3. $C_{13}H_7OCl$ requires C, 72·7; H, 3·3%).

The following reactions were carried out in similar manner except where otherwise stated.

*2-Chlorofluorenone.*—Crude methyl 4-chlorodiphenyl-2-carboxylate (b. p. 185—195°/20 mm., 320°/760 mm.) was obtained in 29% yield from diazotised methyl 5-chloroanthranilate (46·5 g., 0·25 mol.) and benzene. Hydrolysis of the ester gave *4-chlorodiphenyl-2-carboxylic acid*, which crystallised from dilute alcohol in needles, m. p. 157° (Found: C, 67·4; H, 4·0. $C_{13}H_9O_2Cl$ requires C, 67·1; H, 3·9%). Ring closure gave 2-chlorofluorenone, m. p. 123° (Found: C, 73·2; H, 3·5; Cl, 16·3. Calc. for $C_{13}H_7OCl$: C, 72·7; H, 3·3; Cl, 16·5%). Courtot and Vignati (*Compt. rend.*, 1927, **184**, 1179) and Courtot (*Ann. Chim.*, 1930, **14**, 5) record m. p. 123° and Chanussot (*Anal. Asoc. Quim. Argentina*, 1927, **15**, 216) records m. p. 125—126°.

*3-Bromofluorenone.*—Diazotised methyl 4-bromoanthranilate (23 g., 0·1 mol.) and benzene gave crude methyl 5-bromodiphenyl-2-carboxylate (b. p. 185—195°/20 mm.) in 25% yield, which on hydrolysis yielded *5-bromodiphenyl-2-carboxylic acid*; this separated from dilute alcohol in needles, m. p. 172° (Found: C, 56·4; H, 3·2. $C_{13}H_9O_2Br$ requires C, 56·3; H, 3·2%). Ring closure yielded 3-bromofluorenone, m. p. 161° (Found: C, 60·0; H, 2·8. Calc. for $C_{13}H_7OBr$: C, 60·2; H, 2·7%). Montagne and van Charante (*Rec. trav. chim.*, 1913, **32**, 172) describe two forms of 3-bromofluorenone, m. p. 162·5° and 165·5°. Bardout (*Anal. Asoc. Quim. Argentina*, 1934, **22**, 123) gives m. p. 165°, Miller and Bachman (*loc. cit.*) m. p. 162°.

*2-Bromofluorenone.*—From diazotised methyl 5-bromoanthranilate (57·5 g., 0·25 mol.) and benzene, crude methyl 4-bromodiphenyl-2-carboxylate (b. p. 185—200°/20 mm.) was obtained in 29% yield. The free 4-bromodiphenyl-2-carboxylic acid obtained on hydrolysis melted, after crystallisation from dilute alcohol, at 164° (Found: C, 56·5; H, 3·1. Calc. for $C_{13}H_9O_2Br$: C, 56·3; H, 3·2%). Courtot (*Ann. Chim.*, 1930, **14**, 137) gives m. p. 165°. The 2-bromofluorenone obtained on ring closure melted at 150° (Found: C, 60·5; H, 2·7. Calc. for $C_{13}H_7OBr$: C, 60·2; H, 2·7%). Schmidt and Bauer (*Ber.*, 1905, **38**, 3751, 3767) record m. p. 134°, Courtot and Vignati (*Bull. Soc. chim.*, 1927, **41**, 58) m. p. 142—143°, Gomberg and Pernert (*loc. cit.*) m. p. 149°, and Thurston and Shriner (*loc. cit.*) m. p. 146°.

*2-Nitrofluorenone.*—The reaction between diazotised methyl 5-nitroanthranilate (49 g., 0·25 mol.) and benzene gave crude methyl 4-nitrodiphenyl-2-carboxylate in 7% yield. Double the usual quantity of hydrochloric acid was used during the diazotisation, which was effected with solid sodium nitrite. The crude nitrodiphenylcarboxylic ester was extracted from the product, after removal of the excess of benzene, with light petroleum (b. p. 80—100°). Evaporation of this extract left a residue of the crude ester, which on hydrolysis yielded *4-nitrodiphenyl-2-carboxylic acid*; this, purified by sublimation in a vacuum, separated from

dilute alcohol in needles, m. p. 173° (Found: C, 64·1; H, 3·6. $C_{13}H_9O_4N$ requires C, 64·2; H, 3·7%). Ring closure gave 2-nitrofluorenone, m. p. 219° (Found: C, 69·2; H, 3·0. Calc. for $C_{13}H_7O_3N$: C, 69·3; H, 3·1%). Schultz (*Annalen*, 1880, **203**, 103) records m. p. 220°, Ullmann and Mallet (*Ber.*, 1898, **31**, 1696) m. p. 218·5° (corr.), and Diels (*Ber.*, 1901, **34**, 1759) m. p. 222—223° (corr.).

*Action of Diazotised Methyl Anthranilate on Chloro- and Bromo-benzene.*—Reactions were carried out, as described above, methyl anthranilate (50 g., 0·33 mol.) being used with chloro- and bromo-benzene. In the former case a mixture of methyl 2′- and 4′-chlorodiphenyl-2-carboxylates (b. p. 180—200°/20 mm.) was obtained in 17% yield. The mixture of acids obtained on hydrolysis was converted by ring closure into a mixture of 4- and 2-chlorofluorenone. In similar manner the reaction with bromobenzene gave a mixture of methyl 2′- and 4′-bromodiphenyl-2-carboxylate (b. p. 180—200°/20 mm.) in 13% yield. A mixture of the two acids was obtained on hydrolysis and, on ring closure, a mixture of 4- and 2-bromofluorenone. Attempts to separate the constituents of these mixtures were only partly successful.

*4′-Chloro-2-methyldiphenyl.*—*p*-Chloroaniline (25·5 g.), diazotised in the normal manner, was added to toluene (250 c.c.), and the mixture vigorously stirred at about 5° while aqueous sodium hydroxide (30% solution) was added gradually until alkaline. Steam-distillation of the product gave, in addition to recovered toluene, a mixture of chloromethyldiphenyls, from which 4′-chloro-4-methyldiphenyl (m. p. 122°) separated. Redistillation of the liquid residue, which comprised the greater part of the product, gave *4′-chloro-2-methyldiphenyl* as a clear refractive liquid, b. p. 288—290° (Found: C, 77·1; H, 5·3. $C_{13}H_{11}Cl$ requires C, 77·0; H, 5·4%). A portion of this chlorohydrocarbon was boiled under reflux with aqueous potassium permanganate for 10 hours. After treatment of the solution with sulphur dioxide *4′-chlorodiphenyl-2-carboxylic acid* separated, which crystallised from dilute alcohol in needles, m. p. 161° (Found: C, 67·2; H, 4·2. $C_{13}H_9O_2Cl$ requires C, 67·1; H, 3·9%). Ring closure with sulphuric acid at 50° gave 2-chlorofluorenone, m. p. 123° alone and in admixture with the compound derived from 4-chlorodiphenyl-2-carboxylic acid.

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## 26. *Nitrosoacylarylamines. Part I. The Decomposition of Nitrosoacetanilide in Solution.*

By E. C. Butterworth and D. H. Hey.

In continuation of previous work on similar lines (Grieve and Hey, J., 1934, 1798; 1935, 689) a quantitative study is made of the decomposition of nitrosoacetanilide in solution by measurement of the rate of evolution of nitrogen. Attention is directed to the influence of concentration and of temperature on the reaction in benzene solution, and also to the reaction in a variety of solvents. The energy of activation for the reaction in benzene solution is found to be of the order of 22,000 cals. The results are in agreement with the representation of the primary reaction as a non-ionic decomposition into free radicals and molecular nitrogen.

Bamberger (*Ber.*, 1897, **30**, 366) showed that, when nitrosoacetanilide is dissolved in benzene, diphenyl is formed with liberation of nitrogen: $Ph{\cdot}N(NO){\cdot}CO{\cdot}CH_3 + C_6H_6 \longrightarrow Ph{\cdot}Ph + N_2 + CH_3{\cdot}CO_2H$. Similar reactions have been carried out with nitroso-*p*-bromoacetanilide (Hantzsch and Wechsler, *Annalen*, 1902, **325**, 242), and with nitrosoaceto-*p*-toluidide (Kliegl and Huber, *Ber.*, 1920, **53**, 1655), but, apart from these instances, the reaction had received scant attention. Grieve and Hey (J., 1934, 1798) carried out a series of reactions between nitrosoacetanilide and various aromatic liquids and showed the close relationship between these reactions and those of the aryl diazoates, previously studied by Gomberg and his co-workers (*J. Amer. Chem. Soc.*, 1924, **46**, 2339; 1926, **48**, 1372), which may be represented thus: $Ph{\cdot}N_2{\cdot}OH + C_6H_6 \longrightarrow Ph{\cdot}Ph + N_2 + H_2O$. In particular it was shown that in both reactions the normal rules

of aromatic substitution do not hold and that reaction invariably proceeds at the aromatic nucleus at the ortho- and/or para-position with respect to any group which may be present. For this and other reasons (see Grieve and Hey, *loc. cit.*; Hey, J., 1934, 1966) it was suggested that these reactions were non-ionic in type and took place through the formation and transient existence of free radicals. More recently attention has been given to the reactions of nitrosoacetanilide by Waters (J., 1937, 112), who showed (*a*) that in many solvents nitrosoacetanilide decomposes with evolution of carbon dioxide as well as nitrogen, and (*b*) that metallic elements may be attacked during the reaction, even in the presence of an excess of calcium carbonate. These results supply strong confirmatory evidence in support of a free-radical mechanism, on the basis of which the decomposition of nitrosoacetanilide should now be more correctly represented thus:

$$Ph{\cdot}N(NO){\cdot}CO{\cdot}CH_3 \longrightarrow Ph{\cdot} + N_2 + CH_3CO{\cdot}O{\cdot} \qquad CH_3{\cdot}CO{\cdot}O{\cdot} \longrightarrow CH_3{\cdot} + CO_2$$

The reactions of nitrosoacetanilide in organic solvents usually take place at a conveniently measurable speed at about room temperature and quantitative studies have been carried out on the rate of evolution of nitrogen * (Grieve and Hey, *loc. cit.*). With all the solvents employed, the reaction was unimolecular in type and the velocity constants were all of the same order, thus supporting a mechanism of primary dissociation into free radicals and molecular nitrogen. The quantitative study of the reaction is now extended to include (*a*) an examination of the influence of concentration and temperature with benzene as solvent, and (*b*) the use of other solvents.

*Influence of Concentration.*—In order to ascertain the influence of concentration on the decomposition of nitrosoacetanilide in benzene solution experiments were carried out at 20°, in groups of three with the same sample of nitrosoacetanilide, and concentrations were varied from 2 g. to 20 g. of nitrosoacetanilide in 100 c.c. of benzene. The apparatus and the experimental procedure have been described previously (Grieve and Hey, *loc. cit.*, p. 1805). In all these and subsequent experiments, which were carried out in duplicate or triplicate, the benzene was saturated with nitrogen before use and all volumes recorded are corrected. The rate of evolution of nitrogen was observed during about six hours and the final volume of nitrogen was measured after the lapse of at least 24 hours. The yield of diphenyl formed was determined in each case. It was found that, as the concentration of nitrosoacetanilide increased, there was a corresponding increase in the total volume of nitrogen evolved, but the yield of diphenyl isolated showed a progressive decrease. This is clearly due to the formation of ter- and poly-phenyls in increasing quantity. The formation of these hydrocarbons of higher molecular weight is known to be a characteristic of these reactions (Grieve and Hey, *loc. cit.*; see also Gomberg and Bachmann, *J. Amer. Chem. Soc.*, 1924, 46, 2341; Gerngross and Dunkel, *Ber.*, 1924, 57, 739), and in more concentrated solution the tendency for their formation would be greater. The results of these experiments are in Table I. The small departures from an exact linear relationship must be attributed in part to slight differences in the purity of the nitrosoacetanilide used in different sets of experiments. Reference has been made previously to the difficulty of preparing uniformly pure nitrosoacetanilide (Grieve and Hey, *loc. cit.*), the purity of which may vary from about 95 to 99%. In addition, at the higher concentrations difficulty was experienced in keeping the temperature uniformly constant at 20° owing to excessive evolution of heat during the reactions.

TABLE I.

| Nitrosoacetanilide, g., in 100 c.c. $C_6H_6$. | $N_2$ evolved, c.c. | $N_2$ evolved, %. | Ph·Ph isolated, g. | Yield of Ph·Ph, %. | Nitrosoacetanilide, g., in 100 c.c. $C_6H_6$. | $N_2$ evolved, c.c. | $N_2$ evolved, %. | Ph·Ph isolated, g. | Yield of Ph·Ph, %. |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 248·0 | 90·8 | 1·5 | 80 | 7·5 | 908·3 | 88·4 | 4·7 | 67 |
| 2 | 253·8 | 92·7 | 1·5 | 80 | 9 | 1114·0 | 90·3 | 5·5 | 65 |
| 3 | 371·6 | 90·4 | 2·0 | 71 | 10 | 1200·0 | 87·6 | 5·85 | 62 |
| 5 | 584·7 | 85·3 | 3·6 | 76 | 12·5 | 1544·5 | 90·2 | 6·8 | 58 |
| 5 | 575·9 | 84·1 | — | — | 20 | 2352·5 | 85·9 | 8·75 | 46 |

* The discovery by Waters (*loc. cit.*) of the concomitant evolution of carbon dioxide during the reactions of nitrosoacetanilide does not affect the results of the experiments described by Grieve and Hey (*loc. cit.*; J., 1935, 689), in which nitrometers filled with 40% aqueous potassium hydroxide were used.

It has been previously stated (Grieve and Hey, *loc. cit.*) that, although when 2 g. of nitrosoacetanilide were dissolved in 100 c.c. of benzene about 90% of the nitrogen was evolved and diphenyl could be isolated in good yield, yet when the reaction was carried out on a larger scale it was difficult to avoid the formation of tarry by-products with a consequent considerable reduction in the yield of diphenyl. In an attempt to discover the cause of this discrepancy small- and large-scale experiments were carried out side by side and it is now found that, when special precautions are taken to ensure that, as far as possible, both reactions take place under identical experimental conditions, the same percentage volume of nitrogen is evolved and the yield of diphenyl in the large-scale experiment is only slightly inferior to that in the small-scale experiment. The results obtained in one such set of experiments are in Table II.

TABLE II.

| Nitrosoacetanilide, g. | $C_6H_6$, c.c. | $N_2$ evolved, c.c. | $N_2$ evolved, %. | Ph·Ph, g. | Yield of Ph·Ph, %. |
|---|---|---|---|---|---|
| 2 | 100 | 221 | 81 | 1·5 | 80 |
| 20 | 1000 | 2220 | 81 | 13·5 | 71 |

*Influence of Temperature.*—The effect of temperature on the rate of decomposition of nitrosoacetanilide in benzene solution was studied by observing the rate of evolution of nitrogen from 2 g. of nitrosoacetanilide in 100 c.c. of benzene at four different temperatures. The results obtained are in Table III, in which the figures represent the mean values of measurements carried out in triplicate.

TABLE III.

| | | | | |
|---|---|---|---|---|
| Temp. | 10° | 20° | 30° | 40° |
| $N_2$ evolved, c.c. | 239·0 | 249·0 | 238·7 | 257·9 |
| $k$ | 0·00148 | 0·00459 | 0·0170 | 0·0595 |
| Ph·Ph, g. | 1·0 | 1·5 | 1·35 | 1·3 |
| Yield of Ph·Ph, % | 53 | 80 | 71 | 68 |

The rate of evolution of nitrogen, as expressed in the velocity constant $k$, increases fairly rapidly with increase in temperature, the total volume of nitrogen evolved is not appreciably affected, and the best yields of diphenyl are obtained at 20°. The energy of activation of the reaction, derived from the Arrhenius equation by plotting log $k$ against the reciprocal of the temperature, where $\log k = -1/2{\cdot}303 \times E/\boldsymbol{R}T + c$, is found to be of the order of 22,000 cals.

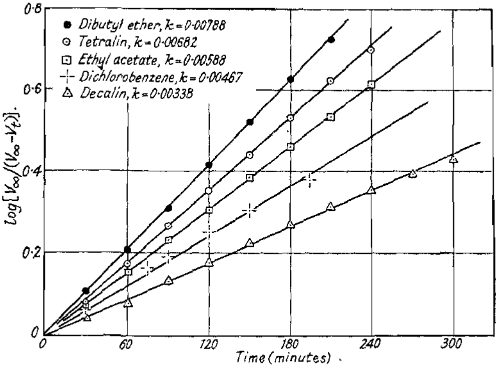
*Influence of Solvent.*—Grieve and Hey (*loc. cit.*) showed that the rates of evolution of nitrogen from solutions of nitrosoacetanilide in carbon tetrachloride, chlorobenzene, and the other aromatic liquids employed differed but little. It was contended that this observation was not fortuitous, but was a direct result of a non-ionic fission into free radicals as the primary process in the reaction. The rates of evolution of nitrogen from solutions of nitrosoacetanilide in chloroform, trichloroethylene, tetrachloroethane, dichlorobenzene (technical), tetralin, decalin, dibutyl ether, ethyl acetate, and diethyl-*o*-toluidine have now been measured at 20° with 2 g. of solute in 100 c.c. of solvent. In each case attention was given to (*a*) the rate of evolution of nitrogen, (*b*) the total volume of nitrogen evolved, and (*c*) the identification of any products formed. In most cases there was evidence of reaction with the solvent, but, owing to the comparatively small amount of nitrosoacetanilide used, the chemical identification of the products was not always possible. The quantitative results obtained are in Table IV, in which the figures represent mean values from experiments in duplicate or triplicate. The value with benzene as solvent is included for comparison.

TABLE IV.

| Solvent. | $N_2$ evolved, c.c. | $k$. | Solvent. | $N_2$ evolved, c.c. | $k$. |
|---|---|---|---|---|---|
| Benzene | 253·8 | 0·00456 | Tetralin | 168·0 | 0·00678 |
| Chloroform | 223·0 | — | Decalin | 184·3 | 0·00332 |
| Carbon tetrachloride | 134·2 | 0·00416 | Dibutyl ether | 169·5 | 0·00790 |
| Trichloroethylene | 53·3 | — | Ethyl acetate | 173·0 | 0·00583 |
| Tetrachloroethane | 156·9 | — | Diethyl-*o*-toluidine | 8·9 | — |
| Dichlorobenzene | 205·7 | 0·00468 | | | |

With this range of solvents the total volume of nitrogen evolved varies within wide limits, thus showing the incidence of reactions between solvent and solute which do not involve the elimination of nitrogen. This is particularly marked in the case of diethyl-*o*-toluidine. In

those cases, however, where a reliable estimation of the rate of evolution of nitrogen could be made, it was again shown that the measured reaction was unimolecular in type and that the velocity constants all fell within a narrow range and were thus not appreciably influenced by the nature of the solvent. The results of individual experiments are represented in the figure,




in which $\log [V_\infty/(V_\infty - V_t)]$ is plotted against $t$, where $V_\infty$ is the final observed volume, and $V_t$ the volume at time $t$. These observations are in agreement with the results and deductions previously obtained in support of a non-ionic fission into free radicals and molecular nitrogen. In the reactions with carbon tetrachloride and trichloroethylene some benzenediazonium chloride was precipitated from solution; with ethyl acetate, some acetaldehyde was formed.

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## 27. *β-Phellandrene.*

By A. Killen Macbeth, Gilbert E. Smith, and Trustham F. West.

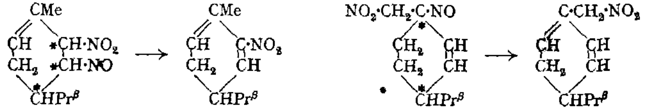
The α-nitrosites of *l*-β-phellandrene from Canada balsam oil and of *d*-β-phellandrene from water-fennel oil have been prepared and examined. Confusion might arise between *d* (or *l*)-β-phellandrene α-nitrosite and *l* (or *d*)-α-phellandrene β-nitrosite, as their melting points lie fairly close together and the specific rotations are of the same sign and of similar magnitude. The mutarotation of β-phellandrene α-nitrosite, however, proceeds slowly and the rotation does not fall to half the initial value. β-Phellandrene is further identified by the conversion of the nitrosite into nitro-β-phellandrene, which on reduction yields cuminal. Oxidation, according to conditions, leads to phellandral or 4-*iso*propyl-$\Delta^2$-*cyclo*hexen-1-one. By these methods the presence of β-phellandrene in Canada balsam oil has been definitely established. Its absorption spectrum in hexane shows a maximum at 2312 A. with log ε 3·96.

The critical examination of the oil of *Eucalyptus cneorifolia* gave evidence of the occurrence of both α- and β-phellandrene in the terpene fractions, and it was therefore desirable to secure authentic specimens of these hydrocarbons for comparison purposes. Water-fennel oil from the fruits of *Phellandrium aquaticum*, L. (Wallach, *Annalen*, 1904, **336**, 1; Berry, Macbeth, and Swanson, J., 1937, 1448) was indicated as a source of *d*-β-phellandrene, and the oil of *Pinus contorta*, which has been reported to consist almost

entirely of *l*-β-phellandrene (*U.S. Dept. Agric. For. Serv. Bull.*, 1913, **119**, 26), was sought as a source of this hydrocarbon, but was unobtainable. A survey of the literature did not disclose any readily obtainable oil which would yield substantially pure *l*-β-phellandrene, but fortunately the recent examination of the oil of *Abies balsamea*, Miller (Smith and West, *J. Soc. Chem. Ind.*, 1937, **56**, 300T) disclosed a new source of the lævorotatory hydrocarbon, and further examination of the carefully fractionated material fully supports the original suggestion that it is *l*-β-phellandrene.

The nitrosites of *l*-α-phellandrene have been comprehensively studied by Read and his co-workers, but the derivatives of β-phellandrene have not received the same detailed attention. Pure *l*-α-phellandrene α-nitrosite has a melting point of 121—122° and a specific rotation in chloroform of + 142·6° (Smith, Hurst, and Read, J., 1923, **123**, 1657), whereas the β-nitrosite has m. p. 105—106° and $[\alpha]_D$ — 156·3° in the same solvent (Smith, Carter, and Read, J., 1924, **125**, 930). The latter values might conceivably be confused with those of a β-phellandrene derivative, for we have found that *d*-β-phellandrene α-nitrosite melts at 102—103° and in chloroform has $[\alpha]_D$ — 165·7° (compare Wallach, *loc. cit.*, p. 44, who recorded m. p. 102°, $[\alpha]_D$ — 159·3°). On the other hand, *l*-β-phellandrene α-nitrosite is found to have m. p. 101—102° and $[\alpha]_D$ + 165·3° in chloroform (compare Smith and West, *loc. cit.*, m. p. 101—102°, $[\alpha]_D$ + 157·9°) and similar values are to be expected in the case of pure *d*-α-phellandrene β-nitrosite. Moreover, since the melting point is not a criterion of optical purity, such physical constants by themselves cannot be regarded as establishing the identity of β-phellandrene; and reports of the occurrence of this hydrocarbon in natural sources which are based on such determinations must be accepted with reserve until further proof is submitted. Thus the occurrence of *l*-β-phellandrene in the oils derived from *Cinnamonum zeylanicum* (Shintre and Rao, *J. Indian Inst. Sci.*, 1932, **15 A**, 84), *Abies nobilis* (Lynn and Nakaya, *J. Amer. Pharm. Assoc.*, 1933, **22**, 305), and *Abies lasiocarpa* (Schwartz, *Amer. J. Pharm.* 1936, **108**, 197) cannot be regarded as established in the absence of further proof.

Since the α- and the β-nitrosite of *l*-α-phellandrene can be converted into identical derivatives, it is evident that the substances are stereoisomers, and Read and his co-workers (*loc. cit.*) have shown that they may be differentiated by observing the specific rotations of their freshly prepared solutions in various solvents. Thus the α-nitrosite gives the highest value in benzene, whereas the β-nitrosite has a maximum specific rotation in chloroform. The mutarotation of the isomers also presents differences. There is a rapid initial fall in the rotation of the α-nitrosite, the original high dextrorotation showing an optical inversion after the lapse of some 24 hours; and a marked lævorotation is finally attained. An initial rapid mutarotation towards zero was also found in the case of the β-nitrosite in all solvents, but optical inversion was observed only in acetone solution: and the maximum change observed in acetone, benzene, and chloroform solutions was, after some 24 hours, followed by a slow decline. The mutarotation changes of α-phellandrene nitrosites (I) are to be associated with the presence in the molecule of three asymmetric carbon atoms, two of which would appear to be susceptible to modification as centres of optical activity through tautomeric change (compare Read, *loc. cit.*; Wallach, *loc. cit.*, p. 19). Similar mutarotation changes are, however, not to be expected in the case of β-phellandrene nitrosite (III), for the molecule contains only two asymmetric carbon atoms, and these do not show the same association as those in the previous case. In chloroform solution both *d*- and *l*-β-phellandrene



(I.) (II.) (III.) (IV.)

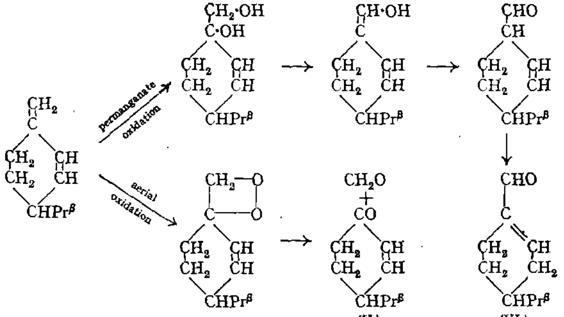
α-nitrosite show only a very slow mutarotation and no optical inversion takes place, since, in fact, the change in the specific rotation does not nearly attain zero. Although

Wallach reported the isolation of a β-phellandrene β-nitrosite (which, very remarkably, was inactive), we have not yet succeeded in preparing such a derivative.

For the further identification of β-phellandrene in Canada balsam oil we have converted the nitrosite into the nitrophellandrene by treatment with sodium ethoxide, and subjected the nitro-compound to reduction. Nitro-β-phellandrene (IV) differs from nitro-α-phellandrene (II) in that it cannot be rectified by distillation; and it also forms a solid compound on treatment with sodium hydroxide solution. The nitro-β-phellandrene derived from the *l*-β-phellandrene of Canada balsam oil was, after purification by steam distillation, lævorotatory, having $[\alpha]_D - 79°$ in alcohol; that derived from *d*-β-phellandrene of water-fennel oil was dextrorotatory, $[\alpha]_D + 107{\cdot}5°$ in the same solvent.

Wallach (*Annalen*, 1895, **287**, 376; *loc. cit.*) has shown that nitrophellandrenes on reduction give rise to carbonyl compounds together with basic products, and the identification of the carbonyl compound establishes the nature of the nitrophellandrene in question. Thus nitro-α-phellandrene gives rise to carvomenthone or carvotanacetone depending on the nature of the reducing agent, whereas nitro-β-phellandrene yields cuminal or dihydrocuminal according to experimental conditions. Structural identity of the phellandrene of Canada balsam oil and of water-fennel oil was thus established by the isolation of cuminal, the derivatives of the experimental aldehyde being identical with those derived from authentic material.

Further proof is found in the oxidation of the β-phellandrene from these sources. Phellandral (VI) was isolated *via* the glycol and identified as the product of permanganate oxidation, whereas aerial oxidation gave rise to 4-*iso*propyl-$\Delta^2$-*cyclo*hexen-1-one (V) (Wallach, *Annalen*, 1905, **343**, 28).




(V.) (VI.)

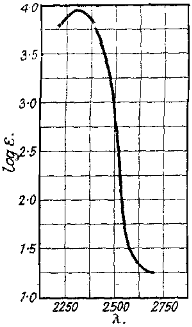
As the present sample of *l*-β-phellandrene from Canada balsam oil may be assumed o be very pure, its absorption spectrum was examined. The main fraction had b. p. 32°/12 mm., $d_{15°}^{15°}$ 0·8497, $n_D$ 1·4800, $\alpha_D - 44{\cdot}1°$ (homogeneous) and $[\alpha]_D^{20°} - 51{\cdot}9°$. Its olution in hexane showed selective absorption of high intensity with a maximum at 2312 A. and log ε 3·96 due to the conjugated ethylene linkages. Allsopp (*Proc. Roy. Soc.*, 1934, *A*, **143**, 624) has shown that 1 : 3-*cyclo*hexadiene exhibits well-defined selective ıbsorption with maxima at 1850 A. (log ε 4·75), 2560 A. (log ε 4·0), and 2680 A. (log ε 3·8). The first maximum is outside the region examined by us, and the other maxima due to he conjugation of the ethylene linkages within the ring are modified to the single naximum at 2312 A. in β-phellandrene, where only one of the conjugated linkages is in he ring itself.

## Experimental.

*l-β-Phellandrene α-Nitrosite.*—The freshly distilled essential oil from Canada balsam, dried ıver sodium sulphate, gave on careful fractionation a product, b. p. 78°/24 mm., which

consisted essentially of *l*-β-phellandrene and had b. p. 178—179°/758 mm., $d_{15°}^{15°}$ 0·8497, $n_D^{20°}$ 1·4800, $\alpha_D$ − 43·2°, $[\alpha]_D^{20°}$ − 50·6° (Smith and West, *loc. cit.*). Redistilled, it gave a main fraction, b. p. 53°/12 mm., $\alpha_D^{20°}$ − 44·1°, $[\alpha]_D^{20°}$ − 51·9°. The absorption spectrum in hexane (figure) is characterised by a maximum at 2312 A., log ε 3·96.

*l*-β-Phellandrene (100 c.c.) was dissolved in light petroleum (600 c.c.), mixed with sodium nitrite solution (210 c.c.), and cooled below 0°, and glacial acetic acid (100 c.c.) at 0° stirred in. After standing for some time in the freezing mixture, the crude nitrosite was filtered off, washed successively with cold water and alcohol, and dissolved in chloroform; to the filtered solution, methyl alcohol was added to precipitate the nitrosite (16·3 g.). The product can be further purified by crystallisation from acetone or by repetition of the chloroform–methyl alcohol treatment. Refrigeration of solutions is desirable on account of the solubility of the nitrosite. Four crystallisations from acetone gave a product, m. p. 101—102°, with $[\alpha]_D^{20°}$ + 160°, but in one case the specific rotation was as high as + 167°. Repurified twice from chloroform and methyl alcohol, a sample had m. p. 100° and $[\alpha]_D^{20°}$ + 169° (*c*, 1·255 in chloroform). In another experiment, repeated treatment with chloroform and methyl alcohol gave a nitrosite, m. p. 101—102°, which had an initial specific rotation in chloroform (*c*, 1·255) of + 165·3° at 25° and showed the following changes when kept in a thermostat at this temperature: after 16 hours, + 130·7°; after 64 hours, + 124·3°; after 92 hours, + 117·1°; after 168 hours, + 105°.




d-β-*Phellandrene α-Nitrosite.*—Water-fennel oil when distilled under reduced pressure yielded, amongst others, the following fractions which gave a strong phellandrene test: (*a*) b. p. 41—47°/7 mm.; $d_{15·5°}^{15·5°}$ 0·8575, $[\alpha]_D$ + 20·8°; (*b*) b. p. 44°/4 mm., $d_{15·5°}^{15·5°}$ 0·8564, $[\alpha]_D$ + 18·85°; and (*c*) b. p. 44—59°/4 mm., $d_{15·5°}^{15·5°}$ 0·8509, $[\alpha]_D$ + 16·16° (Berry, Macbeth, and Swanson, *loc. cit.*). The α-nitrosite prepared from fractions (*a*) and (*b*) as in the preceding case, when purified by repeated treatment with chloroform and methyl alcohol, had m. p.'s ranging from 99° to 102—103° in different experiments and $[\alpha]_D$ values from − 159° to − 165·7°. The nitrosite showed the slow mutarotation characteristic of β-phellandrene α-nitrosite, optical inversion not being experienced. At laboratory temperature the following changes were recorded from an initial $[\alpha]_D$ in chloroform solution of − 162·6°; after 7 days, − 127·5°; after 9 days, − 111·2°; after 12 days, − 97·2°.

d- *and* l-*Nitro-β-phellandrene.*—The nitrosite of β-phellandrene is converted into nitro-β-phellandrene by the action of sodium ethoxide at 30—40° and subsequent heating in a water-bath. The product, poured into cold water and extracted with ether after acidification with dilute sulphuric acid, gave, on removal of solvent, nitro-β-phellandrene as a yellow oil. It gave a reddish-yellow solid, insoluble in alcohol, when treated with half its volume of sodium hydroxide solution (50%). The nitro-β-phellandrene derived from *d*-β-phellandrene α-nitrosite, after steam-distillation, was dextrorotatory, $[\alpha]_D$ + 107·5° (alcohol; *c*, 25), whereas that from the nitrosite of *l*-β-phellandrene was lævorotatory, $[\alpha]_D$ − 78·8° under the same conditions. As the rectification did not involve large amounts of the nitrophellandrene, the rotations may be subject to modification in future work.

*Reduction of Nitro-β-phellandrene.*—It is unnecessary to isolate the nitro-β-phellandrene for reduction, and the solution after treatment of the nitrosite with sodium ethoxide is diluted with a further volume of alcohol, and metallic sodium added under reflux. To a solution of sodium (7·2 g.) in absolute alcohol (150 c.c.), *l*-β-phellandrene α-nitrosite (15 g.) was slowly added, and the thick mass heated in the water-bath for 15 minutes. After the addition of a further volume of absolute alcohol (450 c.c.), sodium (35 g.) was gradually added under reflux. After removal of the greater part of the alcohol with steam the residue in the flask was acidified with dilute sulphuric acid and subjected to steam-distillation; an inactive oil (2·6 c.c.) recovered from the distillate by extraction with ether gave a semicarbazone, m. p. 212° after recrystallisation from methyl alcohol, and a 2:4-dinitrophenylhydrazone, m. p. 244—245° after crystallisation from alcohol–chloroform. These showed no depression of m. p. when mixed with the corresponding authentic derivatives of cuminal.

*d*-β-Phellandrene α-nitrosite similarly gave cuminal on reduction with sodium (compare Wallach, *Annalen*, 1905, **340**, 6).

*Oxidation Experiments.*—(a) A fraction of water-fennel oil (80 c.c.) rich in *d*-β-phellandrene was placed in a quartz flask with water (50 c.c.) and agitated by gentle bubbling of oxygen during irradiation (6 hours) with light from the mercury lamp. Estimation of aldehydes (hydroxylamine method) gave an aldehyde content of approximately 16%, calculated as $C_9H_{14}O$. As the decomposition of the peroxide theoretically gives rise to a molecule of formaldehyde together with a molecule of 4-*iso*propyl-$\Delta^2$-*cyclo*hexen-1-one, this is equivalent to some 3% of the latter. On shaking with 35% neutral sodium sulphite solution (100 c.c.) the liberated sodium hydroxide required 7·3 c.c. of 3N-sulphuric acid for neutralisation. This is equivalent to reaction of 3·02 g. of ketone, a value in good agreement with the deduced percentage. On treatment of the sulphite solution in the usual way 1·1 c.c. of purified ketone were recovered. This had $\alpha_D + 46{\cdot}7°$ and gave a *p*-nitrophenylhydrazone, m. p. 167°, which was not depressed when mixed with an authentic derivative of *d*-4-*iso*propyl-$\Delta^2$-*cyclo*hexen-1-one.

(b) A sample of oil rich in *l*-β-phellandrene (60 c.c.), mixed with water (50 c.c.), was shaken in a 2·5 l. bottle with oxygen and left in sunlight for 2 weeks, oxygen being introduced every few days and the mixture shaken from time to time. Steam-distillation gave 20 c.c. of oil, and a polymerised product remained. The usual sodium sulphite treatment gave 1·5 c.c. of purified lævorotatory ketone, which formed a *p*-nitrophenylhydrazone, m. p. 168° (Found: C, 66·0; H, 6·6. Calc.: C, 65·9; H, 6·7%), and a 2 : 4-dinitrophenylhydrazone, m. p. 137—138°. The m. p.'s were not depressed by the respective derivatives of *l*-4-*iso*propyl-$\Delta^2$-*cyclo*hexen-1-one. Similar results were obtained on oxidation by irradiation as in the case of *d*-β-phellandrene.

(c) The alternative oxidation using 1% permanganate solution was carried out by modification of Wallach's method (*Annalen*, 1905, **340**, 1). 50 C.c. of fraction (*b*) of water-fennel oil (above) were shaken with 1 l. of 1% permanganate solution at 0°. When all the permanganate was decolorised, a further quantity of powdered permanganate was added in small amounts until oxidation was complete, the temperature being maintained at about 0° by the addition of ice. After removal of the manganese sludge, which was well washed, the combined filtrates were concentrated under reduced pressure, and the syrup extracted with chloroform. The glycol remaining on removal of the chloroform was distilled with 10% sulphuric acid (200 c.c.) and 0·5 c.c. of oil was recovered by ether extraction of the distillate. This was identified as phellandral by the 2 : 4-dinitrophenylhydrazone, m. p. 203—204° after crystallisation from alcohol–chloroform. The m. p. was not depressed by the corresponding derivative of *d*-phellandral.

*l*-β-Phellandrene on similar treatment also gave a pale yellow oil, which was identified as phellandral by formation of a semicarbazone, m. p. 203—204°.

We thank Mr. P. A. Berry and Mr. T. B. Swanson for help during the course of the work, and Messrs. Stafford Allen & Sons, Ltd., for facilities afforded to two of us.

Johnson Chemical Laboratories, University of Adelaide.
The Research Laboratory, Stafford Allen & Sons, Ltd., London, E.C. 2.
[*Received, December 13th*, 1937.]

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# NOTE.

## *Molecular Solution Volumes of Optical Isomers. Reply to a Recent Note by William H. Banks.*

By T. S. Patterson and Alexander H. Lamberton.

Banks (J., 1937, 1857) offers some theoretical criticism of our paper on the molecular solution volume of optical isomers (J., 1937, 1453) and has difficulty in attaching significance to the results which we found.

We were, of course, fully aware that we were working very near the limit of experimental error, as indeed is unavoidable in the circumstances, but we are decidedly of opinion that our *practical* results fully justified any conclusions we drew, which, in fact, were very cautious, since the subject is an extremely difficult one, and it should be remembered that each series is a much more elaborate piece of work than might at first sight appear. For these reasons we quoted every experiment of the two series that we made. Nos. V and VI of the second series were the results of the first two experiments carried out by an observer hitherto inexperienced in that *particular* line (although not in related work); and they might perhaps have been

*slightly affected by that inexperience. On this account we might possibly have been justified in omitting them, in which case the concordance of the others would have been decidedly greater, and indeed almost perfect.*

Banks's criticism is fallacious, because he attributes a possible (but improbable) ***maximum error*** of a ***single*** observation to the ***mean*** value of a considerable number of observations expressly designed to reduce this error to a minimum. The mean values used by us are, we think, likely to be decidedly more accurate than any one observation. In any case it is much better practice to estimate the probable error from the experiments themselves—since this is less likely to exclude any of the factors involved, known or unknown—than from *purely theoretical considerations, although we do not wish entirely to disparage the latter.*

We propose to continue the investigation of the subject, when, as we had already decided, we shall try to increase the accuracy of the temperature measurements; but we must enter this immediate caveat against the validity of Banks's criticism.—ORGANIC CHEMISTRY DEPARTMENT, UNIVERSITY OF GLASGOW. [*Received, December 4th*, 1937.]

## Some Problems of Tyrosine Metabolism.

A Lecture delivered before the Chemical Society on March 4th, 1937.

By H. S. Raper, C.B.E., D.Sc., F.R.S.

Tyrosine is one of the amino-acids that has been longest known. It was first isolated in 1846 by Liebig, as a product of the fusion of cheese with caustic potash. Erlenmeyer and Lipp established its constitution and synthesised it in 1882. In proteins which form part of our diet it is not very abundant, and caseinogen, which contains about 6%, is the richest of the food proteins in this amino-acid. In an ordinary mixed diet probably not more than 3 g. are taken daily by the average adult. This is normally readily oxidised. Much larger amounts can be dealt with by the body, for Abderhalden, after taking 150 g., records that no intermediate products of its oxidation were secreted in the urine.

Attempts have been made to find out whether tyrosine should be included in the group of "essential" amino-acids. By this is meant amino-acids which must be supplied in food proteins because they cannot be synthesised in the body. In dogs, Abderhalden failed to get maintenance of body weight when the protein of the diet was replaced by an amino-acid mixture produced by the hydrolysis of caseinogen from which the tyrosine had been largely removed by crystallisation. On the other hand, recent experiments by Alcock have shown that rats will grow satisfactorily on such an amino-acid mixture even when the tyrosine has been removed completely by oxidation with the enzyme tyrosinase. Since there is satisfactory evidence that tyrosine may be produced in the body from another common constituent of proteins, namely, phenylalanine, there seems little reason to doubt that a deficiency of tyrosine in the diet may be made good in this way. The conversion of phenylalanine into tyrosine involves oxidation of the benzene nucleus in the para-position. So far no oxidation system in the body has been found which will bring about this change, though it can be achieved *in vitro* by means of Fenton's reagent.

The general mode of oxidation of amino-acids in the body was first indicated by Otto Neubauer, who, by making use of a non-natural amino-acid (phenylglycine), was able to show that it was converted into phenylglyoxylic acid, which was excreted in the urine:

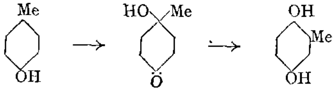
$$C_6H_5\cdot CH(NH_2)\cdot CO_2H \longrightarrow C_6H_5\cdot CO\cdot CO_2H$$

This oxidative deamination of α-amino-acids with formation of the corresponding α-keto-acid has also been demonstrated to occur in the same type of experiment with other amino-acids which do not readily undergo oxidation, *e.g.*, α-amino-γ-phenylbutyric acid, *m*-chlorophenylalanine, and *m*-hydroxyphenylalanine. Enzymes which will bring about this oxidation have since been shown to be present in various organs, notably the kidney, by Kisch and Krebs. More recently an interesting example of this change has been found in certain cases of amentia. In these subjects phenylalanine is not oxidised beyond this first stage and they therefore regularly excrete phenylpyruvic acid in the urine.

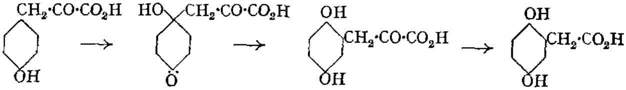
There is good evidence that tyrosine may undergo oxidative deamination in the body. A few years ago a case of abnormal tyrosine metabolism was discovered in Minneapolis by Miss Medes. This subject was admitted into hospital for the treatment of a disease of the muscles, *myasthenia gravis*. It was then discovered by accident that he excreted in the urine daily 2—3 g. of *p*-hydroxyphenylpyruvic acid. Administration of tyrosine caused an increase in the production of this substance, thus clearly indicating its origin. No other example of this metabolic abnormality has been discovered, and it appears to bear no relation to the disease for which the man was originally admitted to hospital. Normal subjects are able to oxidise *p*-hydroxyphenylpyruvic acid with ease, so in this particular case, although oxidative deamination could be effected normally, the mechanism for the next stage of oxidation was defective. This abnormality, which has been named tyrosinosis, has other points of interest in connection with tyrosine metabolism. When phenylalanine was administered to this patient, the excretion in the urine of both tyrosine and *p*-hydroxyphenylpyruvic acid was observed, thus indicating that phenylalanine can be converted into tyrosine in the body. Furthermore, when large amounts of tyrosine

were administered, a small amount of *l*-3 : 4-dihydroxyphenylalanine was found in the urine. This gives proof that nuclear oxidation of tyrosine may occur as well as the more easily demonstrated side-chain oxidation.

Tyrosinosis gives no information about the stages of oxidation subsequent to the production of *p*-hydroxyphenylpyruvic acid. For this we must go to another abnormality of tyrosine metabolism, namely, alcaptonuria. As far back as the 16th century, observations were recorded of patients who passed urine which turned black. In 1858 Boedeker detected a reducing substance in cases of this character, and in 1891 Wolkow and Baumann showed that this reducing substance was homogentisic acid. They also showed that it owed its origin to the tyrosine and phenylalanine of dietary proteins. Subsequently, it has been shown in these cases that homogentisic acid is also produced when *p*-hydroxyphenylpyruvic acid is administered. These subjects have therefore no difficulty in bringing about the first, and some of the subsequent stages in the oxidation of tyrosine. This abnormality of tyrosine metabolism raises two problems of considerable interest. First, how is homogentisic acid produced from *p*-hydroxyphenylpyruvic acid? Secondly, is homogentisic acid on the normal path of tyrosine metabolism, and is alcaptonuria therefore a condition in which homogentisic acid cannot be oxidised because of some deficiency in the normal mechanism for dealing with it, or is the production of this acid a pathological phenomenon, indicating a departure from the normal process of oxidation? The first problem arises because homogentisic acid is 2 : 5-dihydroxyphenylacetic acid, whereas its parent acid, *p*-hydroxyphenylpyruvic acid, is substituted in the 4-position. A reduction of the *p*-hydroxyl group in the latter and re-oxidation in the 2 : 5-position is unlikely, because the reduction of a nuclear hydroxyl group has not yet been demonstrated in the animal body. Further, *o*- or *m*-hydroxyphenylalanine would be expected to give rise to homogentisic acid by oxidation if this mode of formation were possible. But they produce no increase of homogentisic acid excretion in alcaptonuria. The most likely method of formation of this acid is by molecular rearrangement following oxidation. It has been known for many years that when *p*-cresol is oxidised with potassium persulphate, "toluquinol" is produced and this undergoes rearrangement to yield 2-methylquinol:




A similar change may possibly take place in the body when *p*-hydroxyphenylpyruvic acid is oxidised, yielding the corresponding 2 : 5-dihydroxy-acid. This by subsequent oxidation of the side chain—a change that has been demonstrated to occur in alcaptonuria—would give homogentisic acid:




Homogentisic acid.

It should be made clear, however, that, although this type of change has been shown to occur *in vitro* with *p*-cresol, no direct experimental proof of its occurrence with *p*-hydroxyphenylpyruvic acid has been obtainable in the laboratory.

Whether homogentisic acid is a product of tyrosine metabolism in normal human subjects is not easy to determine. They oxidise it readily when given by the mouth, and no evidence of its production when excessive amounts of tyrosine are ingested has been produced except a single instance reported by Abderhalden in which a laboratory assistant excreted a small amount following the administration of 50 g. of tyrosine. If the tyrosine molecule is altered so that the quinonoid rearrangement described above cannot take place, then homogentisic acid is not produced; *e.g.*, *p*-methoxyphenylalanine

is oxidised by the alcaptonuric individual without increase in homogentisic acid excretion. It is chiefly for this reason that it has been suggested that homogentisic acid production is a perversion of normal tyrosine metabolism. This experiment certainly indicates that an alternative path for the oxidation of the benzene nucleus is available even in alcaptonuria, but it does not give conclusive evidence that this path is the one which tyrosine always follows in the normal subject.

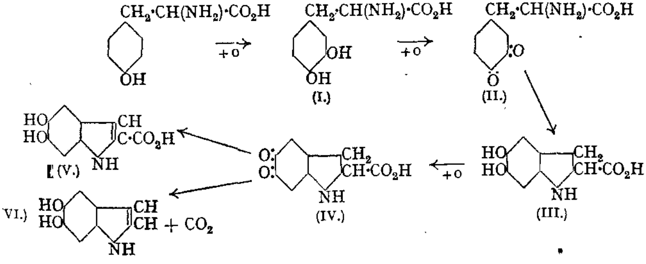
It seems unlikely that further progress in this field will be made until it is possible to isolate enzyme systems which oxidise tyrosine and thus enable a more detailed analysis of the separate stages to be undertaken.

*Pigment Formation from Tyrosine.*

Although the greater part of the tyrosine ingested and not utilised for tissue structure is probably oxidised by one or other of the mechanisms discussed above, the metabolism of some of it may proceed on other lines. One of these results in the production of a black pigment, melanin, which is found principally in hair, skin and the pigment layer of the eyeball.

An enzyme which oxidises tyrosine with the formation of melanin was discovered by Bourquelot and Bertrand in 1895. It was first found by them in certain fungi, but has since been shown to have a wide distribution not only in the vegetable but also in the animal kingdom. Its occurrence in mammals has been demonstrated by Onslow and Pugh, but it is much more commonly found in the invertebrates. The action of the enzyme on tyrosine is not specific. It will act on other monohydric phenols. When tyrosine is the substrate, a series of colour changes is produced. The first visible colour is red and from this various stages of brown are passed through until finally the black, insoluble melanin is deposited.

By modifying the $p_H$ of the reacting system it is possible to demonstrate three separate stages in the oxidation. Tyrosine gives rise to the red pigment in the first stage; in the second this pigment changes into a colourless substance and in the third stage the colourless substance is oxidised to melanin. The second stage is not oxidative, since it will take place in an atmosphere of nitrogen. The first stage is the only one which requires the presence of the enzyme, since the other two will take place in its absence. When the second stage has been completed, the presence of three substances derived from tyrosine can be demonstrated. They are 3 : 4-dihydroxyphenylalanine, 5 : 6-dihydroxyindole, and 5 : 6-dihydroxyindole-2-carboxylic acid. The following scheme has been put forward to explain the production of these three substances from tyrosine:




It involves the production of 3 : 4-dihydroxyphenylalanine ("Dopa") (I), and then of its quinone (II) by oxidation. The quinone next undergoes an intramolecular change with the production of 5 : 6-dihydroxy-2 : 3-dihydroindole-2-carboxylic acid (III). This in turn is oxidised to its quinone (IV), which is the red pigment appearing in the first of the three reaction stages described above. This pigment undergoes further change on

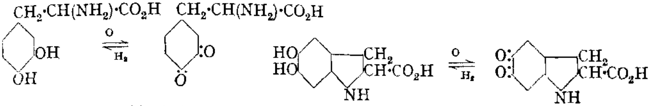
standing, with or without loss of carbon dioxide according to the conditions, and yield 5 : 6-dihydroxyindole (VI) or 5 : 6-dihydroxyindole-2-carboxylic acid (V) respectively Both are oxidisable in the air, especially in alkaline solution, and yield a black pigment Apart from the isolation of (I) as its lead salt and (V) and (VI) by methylation, there is other evidence in favour of this scheme. Dopa is very readily oxidised by the enzyme and gives the same end-products. When monohydric phenols are oxidised by the enzyme they also yield the corresponding *o*-quinones, indicating the likelihood of dopa proceeding next to its quinone (II). Dopa, when oxidised with silver oxide, yields the same products as with the enzyme. The bases tyramine, β-3 : 4-dihydroxyphenylethylamine, and its *N*-methyl derivative all yield the corresponding dihydroxyindoles when oxidised by the enzyme. The red pigment (IV) has been found in the worm *Halla parthenopoea* by Mazza and Stolfi and undergoes a conversion into (V) under the same conditions as in the enzyme action. It may also be reduced catalytically to its dihydro-derivative (III), which will yield (IV) again on shaking in air. The worm *Halla parthenopoea* contains the enzyme tyrosinase, which is no doubt responsible for the production of the pigment. By using β-3 : 4-dihydroxyphenylethylmethylamine as substrate for the oxidation, the red pigment obtained from this may be separated as a crystalline monophenylhydrazone. Similarly the red pigment from *Halla parthenopoea* (hallachrome) may be obtained in the form of a *p*-bromophenylhydrazone. There is thus a considerable body of evidence in support of the oxidation scheme put forward above.

The processes taking place in the last stage of the reaction, which consists in the conversion of 5 : 6-dihydroxyindole and its 2-carboxylic acid into melanin, are at present obscure. Two atoms of oxygen per molecule of indole derivative are utilised, but whether they both remain in the melanin molecule or only one of them is fixed, is undecided. Analyses of animal melanins have yielded different results according to their source. They are amorphous and difficult to purify. At present there is no satisfactory criterion of their purity. Beyond the statement that, in the formation of this pigment from the dihydroxyindoles, quinone formation is a probable first step, it is not possible to go.

Two additional points of interest about the tyrosinase reaction may be referred to. One of these is the stability of hallachrome and the other the accumulation of dopa. Hallachrome made by the action of tyrosinase on tyrosine or dopa is relatively unstable. It undergoes reduction very readily and in the quinone form may serve as a hydrogen acceptor in biological systems. Friedhein has demonstrated that in this way it may facilitate oxidation in the red blood corpuscles of the rabbit. As ordinarily produced in the enzyme action it persists for only a short time, since it changes with moderate rapidity into its corresponding dihydroxyindole. This change is difficult to prevent and this fact makes its isolation from the products of the enzyme action very difficult. On the other hand, as it occurs in the worm *Halla parthenopoea*, it is more stable and may be obtained by suitable means in crystalline form. This difference in stability is at present unexplained. It may be due to adsorption on the components of the epidermis of *Halla*, but trial of other adsorbents in the laboratory has not revealed any with similar stabilising properties.

The accumulation of dopa in the enzyme action is paradoxical. Dopa is much more rapidly attacked by the enzyme than tyrosine and should, therefore, never attain a concentration which would enable it to be isolated. Such, however, is not the case. The point is of interest because its explanation may help us to picture how catechol compounds may be produced under natural conditions. Recent work on this subject by W. C. Evans at Manchester has indicated what is the most likely cause of the accumulation. Two possibilities seemed likely. One was that dehydrase systems occurring in the crude enzyme were using the quinone of dopa as a hydrogen acceptor and so maintaining a certain concentration of dopa in the reacting system. The other was that some later product of the tyrosinase reaction was reducing the dopa quinone and itself being oxidised. Investigation of the ratio, dopa produced : tyrosinase oxidised under different conditions, has shown that the ratio depends on (1) the source of the enzyme, not because of the presence of dehydrases but rather of peroxidase. The latter enzyme diminishes the ratio.

And (2) the presence of reduced hallachrome, which increases the ratio. There appear to be two reversible reactions, (*a*) and (*b*):




(*a*) (II.) (III.) (*b*)

Dopa quinone (II) is reduced to dopa by the dihydroindole derivative (III), into which it is normally transformed [reaction (*a*)], whilst the dihydroindole derivative is oxidised to hallachrome.

This accumulation of dopa in the tyrosinase–tyrosine reaction may be increased still further if ascorbic acid is present. This presumably acts also by reducing dopa quinone. In this or in some similar fashion we have a possible explanation of the mode of formation of catechol derivatives in nature.

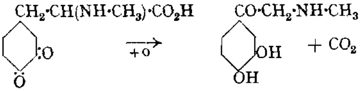
### *Is Melanin of Higher Animals produced from Tyrosine?*

It is common to find tyrosinase and one of its substrates occurring together in lower animals, *e.g.*, the larvæ of the common blow-fly. This makes it reasonable to assume that the melanin produced in these animals is due to the presence of tyrosinase. In mammals, however, tyrosinase is not regularly found in pigmented regions, and the question has arisen, is pigmentation in the higher animals due to the same chemical mechanism as in the lower? There is some evidence that it is. Bloch has shown that in the pigment-forming cells of the skin an enzyme (dopa oxidase) is present which produces melanin from dopa. It is unlikely that the chemical changes involved are different from those which occur when tyrosinase acts on dopa. Dopa does not occur in food proteins, but Miss Medes has shown that it may be produced in the body from tyrosine, and this adds weight to Bloch's theory of pigment production. Furthermore, in certain cases of malignant disease in which pigmented new growths occur in the body—melanotic sarcomata—the urine may contain melanogens which on exposure to the air give rise to melanin. These melanogens give indole reactions and the injection of 5 : 6-dihydroxyindole into rabbits causes them to secrete urine containing a melanogen or melanogens with similar properties to those found in melanotic sarcoma. On the other hand, Eppinger has described a case of melanotic sarcoma in which the amount of melanogen in the urine was increased when the amino-acid tryptophan was administered, whereas tyrosine gave no increase. The nitroprusside reaction was used for the estimation of melanogen. This is not specific for indole derivatives, so it is possible that some substance containing the pyrrole ring but not indole was concerned. Whether it was a derivative of a precursor of melanin or produced by degradation of melanin in the body, cannot be decided, but it does leave open the question as to whether Bloch's scheme of melanin formation is the only one concerned in higher animals.

### *The Origin of Adrenaline.*

It has often been suggested that tyrosine may be the precursor of adrenaline, because of the close structural relationship between these two substances. Many attempts have been made to demonstrate adrenaline formation from tyrosine by the suprarenal gland, but so far without success. Possible intermediates in the process, *e.g.*, dopa, *N*-methyl dopa, and adrenalone, have all failed to give adrenaline when added to the minced gland or circulated in solution through its bloodvessels. Recently, however, Schuler and Wiedermann have shown that thin slices of the gland when placed in tyramine solution will give a slight formation of adrenaline, so that there is biological evidence that tyrosine may be the amino-acid originally concerned in this synthesis. It has also been demonstrated that the enzyme tyrosinase, acting on *N*-methyl dopa, gives rise to a small amount of adrenalone, although the main reaction, as with dopa itself, is pigment formation.

From what we know of the action of tyrosinase, the adrenalone is probably produced from *N*-methyl dopa quinone :



It is not oxidised by the enzyme and hence accumulates. It seems conceivable, therefore, that some such side reaction might become the principal one, if the process leading to indole formation by ring closure were inhibited. In a methylated tyrosine peptide, for instance, this would be possible, since indole formation would be prevented, but not quinone formation.

*Thyroxine.*

Since the elucidation of the structure of thyroxine as a di-iodophenyl ether of di-iodotyrosine it has been apparent that this hormone is probably derived from tyrosine. This evidence has been strengthened by the isolation of 3 : 5-di-iodotyrosine from the thyroid gland and more recently by the proof that *l*-tyrosine and *l*-thyroxine are related configurationally. So far all attempts to convert di-iodotyrosine into thyroxine by enzyme action have failed, so direct biochemical proof is lacking. The synthesis probably requires conditions that can only be found in the living cell and may require not one enzyme, but several. This, therefore, is also a problem of tyrosine metabolism still awaiting solution.

Although in this lecture the problems of tyrosine metabolism have not been exhausted, perhaps sufficient has been said to indicate that even a single amino-acid, out of the twenty or more that proteins may contain, may provide problems that will only be solved by the close co-operation of the chemist and the biologist.

# Bond Character and Interatomic Distance.

A LECTURE DELIVERED BEFORE THE CHEMICAL SOCIETY ON NOVEMBER 18TH, 1937.

By J. MONTEATH ROBERTSON, M.A., D.Sc.

THE precise determination of interatomic distance has become possible during the last 25 years owing to a number of major advances in physical science. Of these, the most important have been the discovery of the diffraction of $X$-rays, and later of electrons, by matter, and the application of quantum theory to the analysis of spectra. Thus we have three powerful and independent methods for studying the distances between atoms in molecules, but none of these methods is capable at present of general application to the whole range of molecules known to chemistry. Each is to some extent restricted to a special field.

The analysis of band spectra, for example, leads to some of the most accurate determinations of internuclear distance, but difficulties of calculation tend to restrict the results at present to certain simple and highly symmetrical types of molecule. Some preliminary figures recently given by Sutherland (*Nature*, 1937, **140**, 239), however, promise an interesting extension of band-spectral methods to the halogenomethanes and other polyatomic molecules which have hitherto been studied only by diffraction methods.

In the diffraction of electrons by gas molecules we have a method with wider application, but the analysis is limited in this case by the comparative meagreness of the experimental data which can be recorded for a given compound. A typical photograph is shown in Fig. I, for which I am indebted to Professor L. O. Brockway, and it will be noted that only a small number of rather diffuse rings are visible. More detail can be distinguished on the negative, but it is seldom that the positions of as many as 10 diffraction maxima can be determined with accuracy against the heavy background. With a molecule of even moderate complexity the number of parameters required to define the structure may actually be greater than the number of intensity maxima recorded on the electron-diffraction photograph, in which case there is, of course, no hope of completely establishing the structure. This limitation, however, does not destroy the usefulness of the method when it is applied to sufficiently simple structures, or even to moderately complex structures, when, by virtue of previous knowledge, they can be described in terms of a few parameters.

A good example is provided by the analysis of benzene (Pauling and Brockway, *J. Chem. Physics*, 1934, **2**, 867) where the C–C distance has been determined with an accuracy which is probably better than 0·01 A., by making use of the geometry of the molecule to limit the number of parameters. But if we knew nothing about the benzene molecule except that it consisted of some arrangement of 6 carbon and 6 hydrogen atoms, it would evidently be quite hopeless to try to determine all the 36 parameters by analysis of the electron-diffraction results. We know that the 6 carbon atoms are equivalent in benzene, not by diffraction experiments, but by the experiments of organic chemistry.

The most powerful method for the metrical study of complex molecules is provided by diffraction experiments on the solid, crystalline material. As the molecules in general possess a fixed and definite orientation in the solid, there is no need to average the diffraction effect over all possible orientations, as in the case of gases. Instead, the structure can be explored in three dimensions. If single crystals of the material are available, there is practically no limit to the number of observations, in the form of intensity measurements on the diffracted beams, which can be made; and each of these observations gives a relation amongst the parameters of the structure. For example, if $a$ is the cell edge, the number of diffracted beams will be proportional to $a^3/\lambda$; so that, as the molecule gets larger, the number of possible observations increases in like proportion, and in any case we can always make this number as large as we please by using a sufficiently small wave-length $\lambda$. This is illustrated in Figs. 2 and 3, which show a small portion of the $X$-ray spectra obtained from a single crystal of oxalic acid dihydrate compared with an exactly similar portion of the spectra from a single crystal of one of the phthalocyanines. In the first case there are 8 atoms in the molecule (including water but neglecting hydrogen), and in the second case there are 41, and it will be seen that the reflections are now about five times as numerous.

There are, however, very considerable difficulties in the interpretation of all these data. Just as in electron-diffraction work, it is usually (though not always) necessary to start with some preconceived model for the molecule, and in the solid we have the additional complication of testing various possible orientations of this model. But the method has this outstanding advantage. Any proposed structure can be tested very exhaustively, and if it is the correct one, the agreements obtained with the experimental observations can be made sufficiently numerous to exclude other possible models. The method is thus extremely suitable for the study of complex structures.

With simple compounds, especially of the light elements, the experimental difficulties of obtaining good single crystals are often very great, and consequently not much accurate *X*-ray diffraction work has been done on such solids. This is unfortunate because it limits the opportunities for making comparisons between the results of the *X*-ray crystal method and those of band-spectra analysis and electron diffraction. Now the last two methods deal with the relative configuration of the atomic nuclei, while the *X*-ray diffraction method deals essentially with the electron distribution. In certain cases, involving multiple bonds, we might anticipate some very small but interesting differences in the results, and it would seem that more work might usefully be done in making accurate comparisons along these lines.

These are, very briefly, the methods which can be employed to measure the distances between atoms in molecules. In the last seven or eight years a very large number of results have been obtained, and it is difficult to make a selection of those which are of most interest. The carbon–halogen distances in simple compounds have been studied very extensively, and the recent results of Brockway (*J. Physical Chem.*, 1937, **41**, 185, 747) on the fluoromethanes show how such measurements lead to a differentiation of bond type which can be correlated with chemical reactivity. Carbon–oxygen and carbon–nitrogen distances have given some unexpected results, and more work requires to be done on such structures. Again, there is the very interesting question of the distances between atoms in neighbouring molecules in the solid state, leading to the detection of hydrogen bonds and other kinds of intermolecular resonance. But the field is too wide, and in this discussion I wish to confine myself chiefly to certain carbon–carbon distances which are of interest in connection with the problem of resonance in certain aromatic and conjugated systems.

There are three normal types of covalent link, called single, double, and triple bonds according as one, two, or three pairs of electrons take part, and the interatomic distance and energy are found to depend on the kinds of atom and the multiplicity of the bond, being approximately constant from one compound to another. Thus Pauling and Brockway (*Proc. Nat. Acad. Sci.*, 1932, **18**, 293; *J. Amer. Chem. Soc.*, 1937, **59**, 1223) have given a table of covalent radii, compiled from crystal-structure and other data, which can be used with a good deal of reliance to predict the distances in many compounds. The revised figures for the first-row elements are as follows.

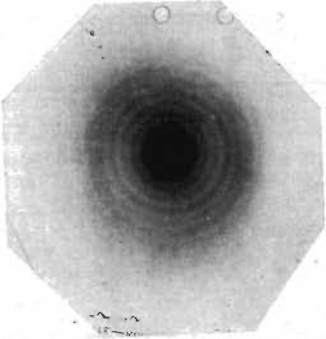
*Covalent Radii* (A.).

| | C. | N. | O. | F. |
|---|---|---|---|---|
| Single bond | 0·77 | 0·70 | 0·66 | 0·64 |
| Double bond | 0·67 | 0·61 | 0·57 | 0·55 |
| Triple bond | 0·60 | 0·55 | 0·51 | — |

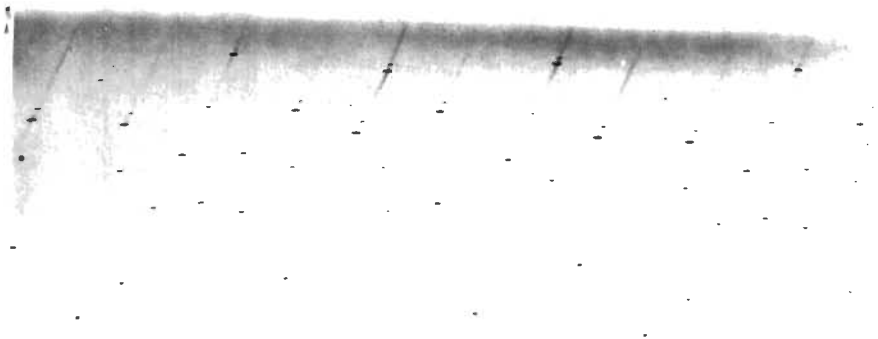
For example, the normal C–C distance is 1·54 A., C=C is 1·34, C—N is 1·47, C=N is 1·28, etc. Very soon, however, the application of this table breaks down. This happens for those structures in which there is no longer a unique way of drawing the bonds, and which can be described in terms of resonance. The most notable examples are, of course, the aromatic compounds, for which it has long been known that the representation in terms of single and double bonds is inadequate.

Before considering this matter in detail, we may survey briefly some results obtained by *X*-ray analysis in which these exceptional distances are displayed. In oxalic acid dihydrate (Robertson and Woodward, J., 1936, 1817) the C–C distance is 1·43 A. The accurate measurement is not easy, and the result may be in error by 0·03 A., but there is no doubt that this " single " bond has undergone a severe contraction from the standard value of

FIG. 1.



*Carbon tetrachloride vapour. Electron diffraction.*



*Oxalic acid dihydrate crystal,* {h0l}: *X-ray spectra.*

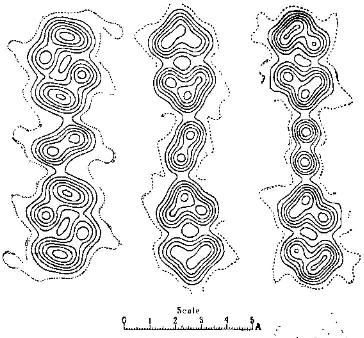
Fig. 3.

l·54 A. The great phthalocyanine molecule provides an excellent example of abnormal listances (Linstead, J., 1934, 1016; Robertson, J., 1935, 615; 1936, 1195; Robertson and Woodward, J., 1937, 219). In the benzene rings the C–C distance averages 1·39 A., the C–C inks connecting these rings to the inner conjugated system are 1·45—1·49 A., while the C–N links of this inner system are 1·34—1·37 A. These figures apply both to free phthalocyanine and to its metal derivatives, and we note that none of these distances can be prelicted by the table of covalent radii—they all lie *between* the single- and the double-bond values.

I wish to mention one other set of structures which are of particular interest in this connection. Although not yet quite fully worked out, all the significant distances have been letermined with some accuracy. The compounds belong to the dibenzyl series (Robertson, *Proc. Roy. Soc.*, 1934, *A*, **146**, 473; 1935, *A*, **150**, 348; Robertson and Woodward, *ibid.*, 1937, *A*, **162**, 568), and the final results of the *X*-ray analysis for three members are represented by the electron-density maps of Fig. 4. These diagrams are projections of the structures along important crystal directions, and although the long axes of the molecules

Fig. 4.

*Dibenzyl.* *Stilbene.* *Tolan.*




ie almost in the planes of the projections, the short cross axes are inclined at high angles of 0—60° to these planes. The benzene rings therefore appear to be distorted, certain pairs f atoms coming so close together in the projection that they are not separately resolved, ut coalesce to form oval concentrations of density. Before the distances and valency ngles can be accurately determined it is necessary to reduce these results to normal proections. But the central pairs of carbon atoms are quite clearly defined, and we can see t once how the valency angle changes from near the tetrahedral value in dibenzyl (single ond) on the left, through stilbene (double bond), where the reduced figure is about 130°, o the accurately linear arrangement imposed by the triple bond of tolan on the right.

These results are an interesting example of a partly direct *X*-ray analysis based upon he use of an isomorphous series of crystals. It is necessary in the first place to assume some nodel for the molecule, and then refine the results by the application of Fourier series nethods. But it is only necessary to assume *one* model. Thus, if we begin with the tetraedral dibenzyl model, the other structures can be obtained directly from the *X*-ray ntensity measurements by successive approximation with Fourier series methods. Or we night begin by assuming the linear tolan model, whereupon the stilbene and dibenzyl tructures could be obtained directly. In practice there are several complications; for

example, the size of the unit cell is doubled in passing from dibenzyl to the other members, and the calculations are difficult and tedious, but the above statement is correct in principle.

When the complete orientations of the molecules are obtained, by the use of other projections, etc., it is found that the distances between the central pairs of carbon atoms are near the standard values given by the table of covalent radii for single, double, and triple bonds. But for the links joining these central atoms to the benzene rings we find abnormal values. In dibenzyl the distance, 1·47—1·50 A., appears to be somewhat less than the true single bond value. In stilbene, at 1·45 A., it is definitely less, while in tolan the distance is only 1·40 A., as small as in many aromatic molecules.

These results, and others of a similar kind, are collected below (in A.), and we see that the internuclear distance, or bond length, can vary considerably in different compounds, and in fact may adopt almost any value between that of a pure single bond and a pure double bond.

| | | |
|---|---|---|
| C—C | diamond, aliphatic hydrocarbons | **1·54** single bond. |
| C—$C_6H_5$ | diphenyl, phthalocyanines | 1·48—1·49 |
| C—$C_6H_5$ | stilbene | 1·44—1·45 |
| C—C | oxalic acid | 1·43 |
| C—C | graphite | 1·42 |
| C—C | naphthalene, anthracene | 1·41 |
| C—$C_6H_5$ | tolan | 1·40 |
| C—C | benzene | 1·39 |
| C=C | stilbene | 1·33—1·35 |
| C=C | ethylene | **1·33** double bond. |
| C≡C | acetylene, tolan | **1·20** triple bond. |

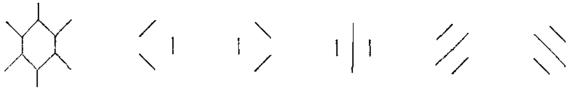
We must now consider the classification of these results, and how they can be used to obtain information regarding the electronic structure of the molecules concerned. Such a classification might in the first place be a purely formal one, enabling some kind of a correlation to be made between different structures. On the other hand, it might be possible to give it more of a theoretical basis, so that when a few standard distances have been measnred experimentally the distances to be expected in other kinds of molecules might be predicted. We now give a brief outline of the attempts which have been made in these directions.

The molecules for which we find the exceptional distances are those which cannot be represented satisfactorily by a single structural formula or bond diagram. To explain their chemical and physical properties it is necessary to assume the simultaneous existence of several structures, and the theory of this " resonance " phenomenon has been developed very largely by Pauling (*J. Amer. Chem. Soc.*, 1932, **54**, 3570; *J. Chem. Physics*, 1933, **1**, 280, 362, etc.). He (*Proc. Nat. Acad. Sci.*, 1932, **18**, 293) also pointed out the importance of interatomic-distance measurements in estimating the relative probability of the several structures which contribute to the normal state of the molecule.

For a molecule such as benzene, three of the bonds of each carbon atom can be accounted for in the usual way (I), as pure single bonds, and these can for the present be neglected in a discussion of the resonance problem. We are then left with what is effectively a system of six univalent atoms between which we can draw three bonds (II).

Now a very extensive mathematical treatment for systems of this kind has been developed (Slater, *Physical Rev.*, 1931, **38**, 1109; Hückel, *Z. Physik*, 1931, **70**, 204; **72**, 310; 1932, **76**, 628; Pauling, *loc. cit.*; Van Vleck and Sherman, *Rev. Mod. Physics*, 1935, **7**, 167; Penney, " The Quantum Theory of Valency," Methuen and Co., 1935). The problem is a very general one and has many applications, *e.g.*, to the cohesion of a system of univalent metal atoms, activation energies, and so on. It is important to notice that this mathematical treatment concentrates on the energy relations of the complex, and that the description of the system in terms of bonds appears to be rather vague. For a system of six univalent atoms there are 15 ways of drawing the bonds, and the actual state of the system will be represented by some superposition pattern of these diagrams. The wave function which corresponds to a diagram with crossed bonds, however, can be shown to be given by the sum or difference of the wave functions of certain of the simpler diagrams without crossed bonds. The number of these simple uncrossed bond diagrams for which the wave functions

are independent is much less, being only five in the case of six univalent atoms. These five independent bond diagrams (II—VI) are termed the "canonical" structures by Pauling.



(I.) (II.) (III.) (IV.) (V.) (VI.)

The wave function for the whole system can be given in terms of these canonical structures by

$$\psi = a_1(\psi_{II} + \psi_{III}) + a_2(\psi_{IV} + \psi_{V} + \psi_{VI})$$

and the coefficients, $a_1$ and $a_2$, of the different sets of structures (which can be grouped together on account of symmetry) have been calculated by Pauling and Wheland (*J. Chem. Physics*, **1933**, 1, 362).

Pauling, Brockway, and Beach (*J. Amer. Chem. Soc.*, 1935, **57**, 2705) now define the fractional character of a given bond in terms of the coefficients of the canonical structures by the relation

$$x = \Sigma' a_i^2 / \Sigma a_i^2$$

the primed sum being taken over those structures in which there is a bond between the atoms in question. Hence for each structure they assess the probability of there being a bond between the atoms, and sum the result.

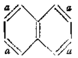
The bond character for a few simple substances like benzene can be derived in this way and an empirical relation established between interatomic distance and bond character. In calculating the bond character of benzene and graphite, however, Pauling, Brockway, and Beach actually employ a simpler definition than that given above, by taking only a linear sum of the non-excited canonical structures. Thus in benzene, by giving equal weights to the two Kekulé structures, the bond character is half single and half double, or 1·5, and in graphite, by considering many structures of the type $\genfrac{}{}{0pt}{}{C}{C}{>}C{=}C$ the bond character is 1·33. The valency of carbon is simply divided by the number of available bonds.

The C–C distances in benzene and graphite are accurately known, and so are the distances for pure single and pure double bonds. When these distances are plotted against the bond character given by the above methods it is found that a smooth curve can be drawn through the four points. By the use of this empirical relation, Pauling, Brockway, and Beach have discussed and classified a large number of interatomic distance measurements in relation to the information they give regarding the degree of resonance in the molecules concerned. By a suitable translation and change of scale, they apply the curve to discussing the resonance effect on bonds other than C–C bonds, as for example the C–Cl bonds in carbonyl chloride and the chloroethylenes. They find a small amount of double-bond character in the C–Cl bonds when conjugated to a double bond, a fact which can be correlated with chemical reactivity; C–N bonds are also discussed, and in urea, for example, they appear to have about 20% double-bond character.

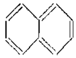
We see, therefore, that this conception of the fractional character of a bond enables us to classify the results of interatomic-distance measurements and draw conclusions regarding the relative extent of the resonance phenomenon in different molecules. We now come to the more quantitative aspect. Can this classification be used as a basis for predicting the distances in other molecules? A large amount of mathematical work has been done on the resonance problem in recent years, and it should be possible to employ accurate distance measurements as an experimental test of this work.

Take, for example, the naphthalene molecule. If we assume a linear sum of the non-excited canonical structures (VII–IX) we see that all the bonds except *a* are double bonds for $\frac{1}{3}$ of the time, but *a* is a double bond for $\frac{2}{3}$ of the time. The fractional characters are

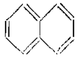
thus 1·33 and 1·66, corresponding to distances, on Pauling's curve, of 1·42 and 1·38 A., the results being shown by (X). It is possible, however, to go further and take account of the




(VII.)



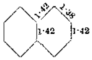
(VIII.)

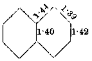


(IX.)

excited structures as well, on the basis of their coefficients in the approximate wave function for the naphthalene molecule calculated by Sherman (*J. Chem. Physics*, 1934, **2**, 488). The results are then given by (XI).

(X.)




(XI.)

The experimental measurements on the naphthalene molecule (referred to more fully later) are hardly yet of sufficient accuracy to reflect such small distortions from a regular structure, but such results as have been obtained are not in favour of (X) or (XI). Although the method of defining fractional bond character outlined above has proved useful in the general discussion of resonance in related groups of molecules, it would appear to be unsuitable for quantitative predictions of the kind now required. This failure may perhaps be ascribed to a certain over-emphasis on the physical significance of the canonical structures. We have already seen that the mathematical treatment of these problems concentrates on the energy relations, and that the description in terms of bonds is rather vague. The canonical structures are the different ways of drawing the bonds between an imaginary set of univalent atoms that lead to the simplest independent set of wave functions, and the complete wave function will be some linear combination of these. But this complete wave function might also be expressed as a different combination of another set of structures, some of them involving crossed bonds, and these two expressions would not necessarily lead to the same value for the fractional bond character between a given pair of atoms.

But whatever set of structures are used to define the problem, the energy levels calculated from them must be invariant, and Penney (*Proc. Roy. Soc.*, 1937, *A*, **158**, 306) has recently employed a new definition of bond " order " based on the energy relations. This treatment is not so general as Pauling's, being restricted at present to C–C bonds only, but it has led to some very promising calculations of distance, and these are also in agreement with other recent calculations by Lennard-Jones (*Proc. Roy. Soc.*, 1937, *A*, **158**, 280, 297) by the method of molecular orbitals.

In the benzene problem, Pauling and Wheland (*J. Chem. Physics*, 1933, **1**, 362) find that the energy of the normal state of the molecule is given by $W = Q + 2{\cdot}61J$. Here the energy of the electrons forming the system of single bonds (I) is neglected, and certain simplifying assumptions are made. $Q$ is the additive Coulomb integral, which we can neglect, and $J$ is the exchange integral—the two types of binding energy which appear in the hydrogen molecule problem (Heitler and London, *Z. Physik*, 1927, **44**, 455). These integrals themselves cannot be calculated for a system of carbon atoms, but the energy can be expressed in terms of them. If we take, for example, a single Kekulé structure (II), when the atoms are linked by a bond the contribution to the energy is $J$, and when they are not so linked the interaction is expressed by $-\frac{1}{2}J$. (The non-binding interaction of $-\frac{1}{2}J$ can also be derived from a consideration of the results of the hydrogen molecule problem; see Penney " Quantum Theory of Valency," Chapter II, Methuen and Co., 1935.) Hence for one Kekulé structure, the energy, the Coulomb integral being neglected, is $W = 3J - 1{\cdot}5J = 1{\cdot}5J$, and the difference between this result and the value of $2{\cdot}61J$, calculated by Pauling and Wheland by solving the secular equation for the complete system, represents the " resonance energy " for benzene. The existence of this resonance energy can be demonstrated from the thermochemical data (Pauling and Sherman, *J. Chem. Physics*, 1933, **1**, 606).

Now Penney defines the " order " of a bond in terms of the exchange integral in such a

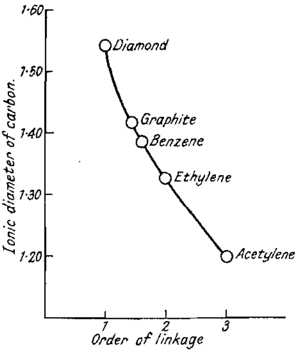
ay that the energy relation is satisfied. If there are $k$ equivalent pairs of neighbouring rbits, the average energy per pair is $W/k$, and if $p$ is the bond order

$$W/k = p(J) + (1 - p)(-\tfrac{1}{2}J)$$
r
$$p = (1 + 2W/kJ)/3$$

A more profound definition of $p$, based on the Dirac vector model, is possible, for which eference should be made to Penney's paper (*Proc. Roy. Soc.*, 1937, *A*, **158**, 306). But we e that if $W$ can be calculated in terms of $J$, the bond order may be obtained immediately rom the above relation. If the exchange energy for benzene were $1{\cdot}5J$, as for a single Kekulé structure, the bond order would be 0·5, or, adding 1 for the system of single bonds, ·5, as in the calculations of Pauling, Brockway, and Beach. But the energy state for the omplete system is actually $W = 2{\cdot}61J$, which gives a bond order of 1·623. Penney's efinition thus makes the bond order in benzene greater than 1·5 on account of the extra esonance energy. For graphite the calculations are more involved, but by a method of uccessive approximation Penney obtains an xchange energy per atom in the sheet of $\cdot 27J \pm 0{\cdot}01J$, which gives an energy per bond f $0{\cdot}18J$, and a bond order of 1·45.

We can now plot these calculated bond rders against the measured distances in iamond graphite, benzene, and ethylene (Fig. ), and it is found that a smooth curve can be rawn through the points, and that this curve ow passes through the triple-bond point acetylene) as well. If the C–C bond order for ther substances can be calculated, the internuclear distance to be expected may be stimated from this relation.

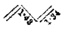
FIG. 5.



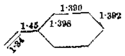

*The ionic diameter of carbon as a function of bond order (Penney).*

Benzene and graphite were chosen as intermediate points to define this curve because in hese substances the bonds are all equivalent, nd the calculations are relatively simple. When the bonds are not necessarily all equivalent the calculations become more difficult, ut Penney has recently obtained definite esults for a number of structures. Without escribing these detailed calculations, we may ow compare the results with the experimental measurements given earlier in this discussion.

The calcnlated distances for some typical cases are shown by (XII)—(XIV). The esonance effect on a single bond situated between two double bonds is illustrated by utadiene, where the length of 1·43 A. is in exact agreement with the molecular orbital alculations of Lennard-Jones (*loc. cit.*, p. 280). There do not appear to be any accurate xperimental data on butadiene at present, but in oxalic acid, where the C–C bond provides he path of conjugation between the two carboxyl groups, the situation is evidently similar, nd for this structure the measured length of the link is 1·43 A.



(XII.)



(XIII.)

(XIV.)

Phenylethylene has been chosen for the calculation of the effect on a single bond conugated between a double bond and a benzene ring. The contraction of the single bond is ow not quite so great, the length obtained being 1·45 A. This figure is in quantitative greement with the experimental measurements on stilbene.

In both butadiene and phenylethylene the calculations show that the double bonds are increased by only 0·01 A. from the measured value of 1·33 A. in ethylene. Similarly, in phenylethylene, the links in the benzene rings deviate only very slightly from the normal values. These small effects are quite beyond the reach of experiment at present, the stilbene measurements, for example (Robertson and Woodward, *Proc. Roy. Soc.*, 1937, *A*, **162**, 568), merely indicating approximately regular benzene rings of the usual size.

Penney's calculations for the naphthalene molecule, based upon an extension of Pauling's treatment of resonance energies, are shown in (XIV), and we note that they differ from the previous results (X and XI) in predicting the greatest length for the central bond between the rings. The calculations are complicated, and may not even yet be very accurate. The mean value of 1·40 A., however, is in good agreement with the experimental value of 1·41 A. The deviations from this mean are of small order, but it is interesting to note that when the experimental work was reported (Robertson, *ibid.*, **1933**, *A*, **142**, 674, 686) one of the Fourier projections gave a value of 1·44 A. for the middle link. This may be due to experimental error, but the result indicates that a more accurate examination would now be useful.

The importance of diffraction measurements as an aid to the determination of chemical structure, in indicating the symmetry and shape of complex molecules, the absolute configuration of geometrical isomers, and so on, has often been stressed. In this discussion I have tried to show, on the other hand, how really accurate measurements of interatomic distance by these methods can be used as an experimental test of some of the new developments in theoretical chemistry which are becoming so important.

# *The Le Chatelier Memorial Lecture.*

## HENRY LE CHATELIER,
## 1850—1936.

A MEMORIAL LECTURE DELIVERED ON OCTOBER 28TH, 1937.

By CECIL H. DESCH, D.Sc., Ph.D., F.R.S.

IN accordance with the custom of this Society on the death of one of its distinguished Foreign Members, we commemorate to-day a great French chemist whose career, singularly clear and consistent in the principles by which it was guided, covered a very wide range, so that the student of chemistry meets with his name in what might at first appear as very different fields. A great physical chemist, Le Chatelier applied the principles of the science to a variety of problems, many of which were presented to him by industry. As a teacher and for many years an acknowledged leader, he exercised a profound influence on the academic and industrial life of France, whilst his character and achievements were held in honour by men of science of many nations and schools.

Henry Louis Le Chatelier (the second name is not used in his publications) was born in Paris on the 8th of October, 1850. His father and mother came from families which numbered among them men of distinction in science, in exploration, and in art. His father, Louis Le Chatelier, had been trained in the École Polytechnique and the École des Mines. Holding a position in the Crédit Mobilier, he was actively associated with many industrial advances, notably with the construction of railways in France, Northern Spain, and Austria; with the establishment of the Siemens-Martin process of steel smelting; and with the development of the Deville process by means of which aluminium was first successfully manufactured on a commercial scale. Having a small private laboratory, he conducted experiments in chemistry, and kept up a close friendship with men of science, including Dumas, Chevreul, Tresca, and Siemens, and above all with Henri Sainte-Claire Deville, whose laboratory at the École Normale he often visited with his son on Sundays. Louis Le Chatelier seems to have had clearly defined ideas of scientific method. He had a love of geometry, but a distrust of mathematical methods when extended beyond what he regarded as their legitimate sphere, an attitude which is reflected throughout in the writings of his son, on whom he sought to impress the need for the clear statement of a problem before attempting its solution, and the avoidance of all superfluous hypotheses.

Henry was the eldest of six children. One of his brothers, Louis, became the technical director of engineering and metallurgical works, another, André, made a reputation as a naval engineer and was a pioneer of autogenous welding, and a third, Alfred, after several missions in Africa, became professor of Mussulman Sociology in the Collège de France, and was one of the inspirers of French colonial policy. The mother, née Durand, was an ardent catholic of the school of Lamartine, who devoted herself entirely to the upbringing of her family. It was she who mainly influenced him in his earlier years, impressing on him, as he says, a love of order, both in society and in scientific thought, producing in him a strong distaste for revolutionary ideas of every kind, whether in the domain of politics or in that of atomic physics.

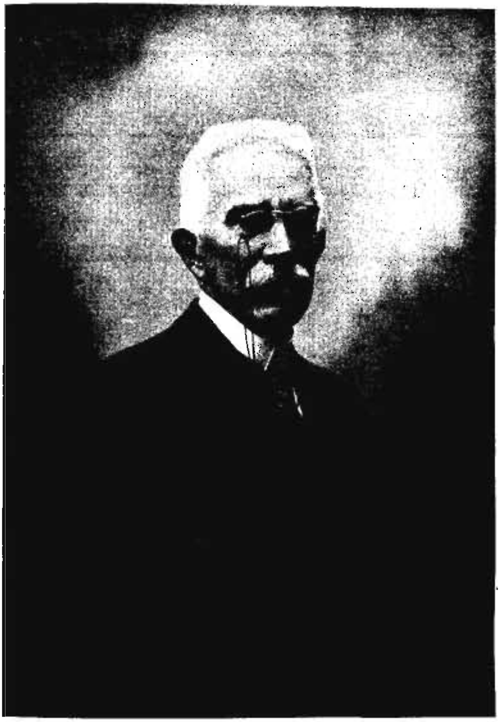
After his schooling at the Collège Rollin, of which he always spoke with affection, he entered the École Polytechnique in 1869. The standard of teaching does not seem to have been high, but he was at least encouraged in the study of geometry. Moreover, some of the students showed independence of thought, and inspired by the ideas of Auguste Comte, Le Chatelier and a friend, Pistor, attempted to re-write the official course in physics, eliminating all metaphysical ideas, such as that of force. His studies were interrupted by the necessity of serving as a sub-lieutenant during the siege of Paris, but in 1871 he passed into the École des Mines, in order to be trained for the engineering service of the State. Here, besides taking the professional courses, he voluntarily attended other lectures, including those of Sainte-Claire Deville at the Sorbonne and of Étienne Marey at the Collège de France, while pursuing literary studies under a professor named Charpentier.

On graduating from the École des Mines, he took part in a government mission to Algeria to report on the possibility of constructing an inland sea in that region, and on returning served for two years as a mining engineer in the Corps des Mines at Besançon. He had, as he tells us, at that time no intention of teaching, but looked forward to a career in administration.

During this period he published one short scientific note—his first communication to the Academy of Sciences—and in view of his later fame as a metallurgist it is interesting to find that it dealt with a metallurgical problem. Tresca had shown that the fibrous character of wrought iron, made by the puddling process, was due to the presence of inclusions of slag or, as it is generally called, " cinder." In order to isolate these inclusions, Le Chatelier adopted a method which had been used by Schloesing for the analysis of cast iron, namely, removal of metallic iron by distillation in a stream of dry chlorine at a dull red heat. A skeleton of the original specimen remained, consisting of these non-metallic inclusions. This method has been revived during the last few years for the study of inclusions in cast irons and in alloy steels.

In 1877, only two years after graduating from the École des Mines, Le Chatelier was recalled to the same institution by its director, the famous geologist, Daubrée, to become professor of general chemistry. He tells us that his only qualification was a good report of his work in chemistry in the College examinations, but that there was no engineer in the Mining Corps who was better qualified. However, he entered seriously on the duties of the post, and determined to undertake research. His father had died some years before, and he was at a loss to know how to choose a subject for investigation. He approached Sainte-Claire Deville, who told him, rather scornfully, that the question was absurd; that one had only to begin work in a laboratory to find oneself surrounded by problems, the only difficulty being to select from among them. This counsel not being very helpful, he remembered that his maternal grandfather, Pierre Durand, had been a friend of Vicat, the first investigator of synthetic hydraulic cements, and that when examining the specimens left by Vicat at the École des Mines he had consulted the literature of the subject, and had found that a scientific knowledge of the constitution of this class of materials was completely lacking. This decided his choice of a thesis for his doctorate. Even before starting this work, however, he began, in collaboration with his senior colleague F. E. Mallard, the studies of fire-damp in mines to which reference will be made later.

His first paper on the setting of cements appeared in 1882, after he had been working on the subject for two years, but for an account of the work it is better to turn to its full presentation in his thesis, submitted in 1887, and republished in 1904 with further additions under the title " Recherches expérimentales sur la constitution des mortiers hydrauliques." The views as to the constitution and setting properties of cements here set forth have been extended and supplemented by later workers, but they remain unchanged in essentials. Being well aware of the complex nature of Portland and similar calcareous cements, and having the classical work of Vicat on pozzolanic materials as a guide, Le Chatelier decided to begin with a simple example, that of plaster of Paris. Lavoisier had shown that in the process of " burning " gypsum water was lost, and that in the course of setting the solid was again hydrated, so that the final product was gypsum, with the crystals closely entangled with one another. The dehydration of gypsum had been found by Payen to occur at 300°. Repeating the experiment, and adopting Regnault's plan of immersing a thermometer in the mass and observing the temperature at which an arrest occurred on heating, Le Chatelier found that water was lost at 135°. Payen had recorded the temperature of the furnace in which the mass was enclosed, and not that of the gypsum itself. A small arrest was also noted at 170°, but this was for some time attributed to experimental error. Later (1883), as the same point reappeared in every experiment, the loss of weight was determined, and it proved that only three-fourths of the water was driven off at 135°, the remainder being lost at 170°. There was thus a lower hydrate of calcium sulphate, $CaSO_4,\frac{1}{2}H_2O$, and this proved to be the substance present in normal plaster and not, as Lavoisier had supposed, the anhydrous salt. The hemihydrate was obtained in crystals by heating gypsum in water in a sealed tube at 150°, and was also recognised



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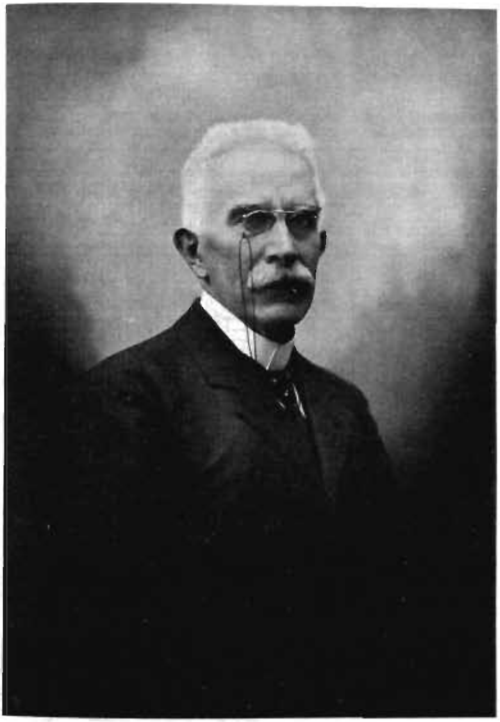

[To face p. 140.

in the incrustations found in marine boilers. It was not clear, however, why the mass should become hard as the result of re-hydration. The solubility of calcium sulphate in water is too low to allow of the whole going into solution and crystallising in the new form, when only sufficient water is present to make the mass pasty. Marignac had observed that if burnt plaster were shaken with water and quickly filtered, a much more concentrated solution was obtained than if the hydrated salt had been taken. The process of setting was thus to be explained, not by the conversion of each particle of the solid hemihydrate into gypsum, but by the production of a highly concentrated solution around each particle, from which the new crystals of gypsum separated, forming an interlocking mass. The crystals are too small for their form to be observed, but by mixing with dilute alcohol in place of water, the process was so retarded that the actual crystallisation could be watched. The formation of hydrated crystals out of contact with the original solid could be seen still more easily by dissolving plaster in a solution of potassium sulphate and then filtering. The solution obtained is so highly supersaturated that the filtered liquid becomes a pasty mass of hydrated crystals.

The next step was to extend this work to calcareous cements, but some experiments were first made with the silicates of barium. The metasilicate, $BaO,SiO_2$,* was prepared in a hydrated form with $6H_2O$, and proved to be identical with crystals previously recorded by Pisani as being formed inside glass bottles containing baryta water. The anhydrous salt, prepared by fusion, set with water like plaster, forming the hexahydrate. An orthosilicate, $2BaO,SiO_2$, was also prepared by fusion, and this reacted with water, giving the same hydrated metasilicate, together with crystals of barium hydroxide. This behaviour gave a clue to the probable mechanism of setting of the calcium compounds. Cement clinker was known to be a complex substance, so the problem was approached synthetically, the compounds of lime, silica, and alumina being first isolated in a pure state and their properties examined. One calcium silicate was already known, $CaO,SiO_2$, and this proved to be inert. The orthosilicate, $2CaO,SiO_2$, required a very high temperature for its preparation, and whilst forming a hard mass on solidification, fell into a loose powder on further cooling. This behaviour had already been observed in certain slags and cements, and the property was now explained as being due to a polymorphic change involving a large expansion of volume. As the disintegrated silicate had no hydraulic properties, but merely formed a mud with water, it was concluded that it played no part in the setting of cement. The analysis of "grappiers" (hard nodular masses often found in hydraulic limes, and resisting slaking with water) suggested that a compound $3CaO,SiO_2$ might exist, but for some time all attempts to prepare it synthetically failed. Calcium chloride was added as a flux, but the product was a new compound, $2CaO,SiO_2,CaCl_2$. However, by decomposing this by superheated steam the tribasic compound was obtained in a nearly pure state. Since it set hard with water without expansion, it was concluded to be the essential constituent of Portland cement. It was identified in cement clinker by the appearance of its crystals in thin sections under the microscope, the mineral constituents surrounding it being considered to have served as a flux during its formation at a high temperature.

Alumina is, however, also present in cement, and as aluminates of several metals were already known, it was probable that this oxide was combined with lime. Three such compounds were prepared synthetically: $CaO,Al_2O_3$; $3CaO,2Al_2O_3$; and $3CaO,Al_2O_3$. All of these set rapidly with water, but formed a less stable mass than the silicates. The next stage was the study of the products of hydrolysis, and it was shown that the final product of the setting of the silicate was $CaO,SiO_2,2{\cdot}5H_2O$, whilst the far more easily soluble aluminates yielded a product which was given as $4CaO,Al_2O_3,12H_2O$, but was later shown by Candlot to contain only three molecules of lime, and its formula was altered accordingly. Iron oxide, although a stable compound $3CaO,Al_2O_3,Fe_2O_3$ was prepared, was found to take no part in the setting. The hydrolysis of the silicate liberated two molecules of lime, which could be recognised as crystals of calcium hydroxide in the cement after setting. The mechanism of setting and hardening was worked out in detail, based on results obtained with plaster and on the formation of an unstable supersaturated

* It is convenient to represent compounds of this kind as being composed of simple oxides.

solution which then deposits the stable products in the form of very fine interlocking crystals. The process was studied in the synthetic compounds and in commercial cements and hydraulic limes, and its identity proved. The thesis contained other important conclusions. For instance, since any excess of uncombined lime in the clinker was found to cause expansion and disintegration on setting, a limit was set to the ratio of bases (lime and magnesia) to acids (silica and alumina), the fact being also indicated that as actual fusion does not occur in the kiln, the reactions are always incomplete, so that the practical limit of lime is below the theoretical. This limit was the first "hydraulic modulus," various values for which have been given by later writers and embodied in specifications. Lastly, the causes of the disintegration of cements after setting are discussed, and it is shown why the presence of free lime causes an increase of volume, whilst the liberation of calcium hydroxide during setting has no such effect.

This memoir, which contains excellent drawings of the several substances, as examined by Sorby's petrological methods, forms the basis of our knowledge of cements, and in all substantial matters it has proved to be correct. The very accurate thermal analysis of the component systems at the Geophysical Laboratory in Washington, which has added greatly to our knowledge, has confirmed the existence of Le Chatelier's three calcium silicates, and the only alteration in regard to the aluminates is the substitution of a 5 : 3 molecular ratio for the 3 : 2 originally given. When it is considered how simple were the experimental means employed, and how complete the results, the investigation must be regarded as one of the classics of inorganic chemistry.

The picture of hardening presented in this work met with some objections. In 1893 W. Michaëlis put forward the view that setting and hardening are colloidal processes, the gradual desiccation of the colloid giving the mechanical strength. This view was never accepted by Le Chatelier, and when a general discussion of the problem was arranged by the Faraday Society in 1919, he maintained his original position, admitting, however, that the crystals might be so minute as to be indistinguishable as such. The difference between the two views then became little more than one of terminology, since *X*-ray experiments show that the colloidal silicates are largely made up of very minute crystals.

Le Chatelier returned on several occasions to the study of cements, concerning himself especially with the improvement of methods of analysis and testing, with the control of manufacture, and with the conditions bringing about the disruption of masses of cement and concrete in air, water, or sea water. His simple apparatus for determining the liability of a cement to disruption, consisting of a split cylinder having two pointers attached, the divergence between which measures the expansion of the cement enclosed in it when immersed in water at 100° for three hours, has been generally adopted. He also carried out many researches on the allied subjects of ceramics and glass.

The research on cements illustrates very clearly Le Chatelier's attitude towards science. Having the social importance of scientific discovery always in view, he refused to recognise any distinction between pure and applied science. His most interesting themes were suggested to him by the needs of industry, whilst he insisted constantly on the importance of the reaction between the two, instancing the origin of the rare-gas industry from the academic investigation by Rayleigh of the anomalies in the density of nitrogen, and on the other hand of the creation of thermodynamics by Sadi Carnot as the result of an attempt to improve steam engines in order to meet English competition.

The research on cements opened up several other lines of work having important results. It became necessary to devise some means of measuring high temperatures, such as that of the fusion of silicates, with much greater accuracy than could be obtained with such crude instruments as those of Wedgwood and Siemens. Antoine Becquerel had proposed in 1830 to make use of the thermoelectric effect originally discovered by Seebeck, and platinum–iron and platinum–palladium couples had been used by Pouillet and by Edmond Becquerel. Regnault, however, made a careful study of these couples and found such irregularities in their behaviour that he condemned the method as being inherently inaccurate. Le Chatelier took up the subject, and found that the irregularities were due to contamination of the one wire by diffusion of the other metal, producing a varying *E.M.F.*, and to the lack of uniformity of the wires themselves, it being possible to produce an

effect even by heating locally a single wire. In 1887, therefore, he proposed the use of a couple composed of one wire of pure platinum and another of an alloy of platinum containing 10% of rhodium. This proved satisfactory, and although many other combinations have been used, this couple remains to-day the international standard. It is interesting to note that, only two days after the reading of the paper describing the new pyrometer, Dr. Ludwig Mond ordered two such couples by telegram, and these, introduced into his works, were the first to be used in industry. In 1890 the couple was introduced into the steel industry by Sir Robert Hadfield. It was, however, not enough to devise a couple of constant properties; the best conditions for use had to be found. The readings were made much more accurate by using an aperiodic galvanometer of the Desprez–d'Arsonval type, whilst the method of calibration by using a number of fixed points, such as the melting points of pure metals and the boiling point of sulphur, was introduced at the same time, making the troublesome comparison of each couple with the air thermometer unnecessary. With these inventions thermoelectric pyrometry became at once a standard method, the applications of which have continually increased. He also concerned himself with optical pyrometry, for the purpose of measuring the temperatures reached in open-hearth steel furnaces. Modifying Cornu's photometer for the purpose, and comparing the radiation from a standard amyl acetate lamp with that to be measured, interposing a red filter, he was able to measure temperatures with greater accuracy than before, giving 1500—1600°, for instance, as the working temperature of the Siemens furnace, whilst previous estimates had been as high as 2000°. Although the instrument itself has been superseded, valuable work was done with it, especially in the determination of the emissive powers of various heated solids, the great variation in which is the principal source of error in industrial measurements with the optical pyrometer when strict black-body conditions are not attained.

Simultaneously with the research on cements, research was being carried on in another field. Work on the explosion of gaseous mixtures was undertaken at the request of a commission appointed in 1877 to examine the best means of guarding against explosions of fire-damp in mines, public opinion having been aroused by a succession of mining disasters. In May 1878, F. E. Mallard and Le Chatelier were asked to study the problem experimentally, and this was the beginning of a long series of researches. That a certain temperature was needed to bring about an explosion was known from the work of Humphrey Davy, but the conditions of propagation of a flame were unknown, and there were no satisfactory methods of determining the proportion of fire-damp in a mine atmosphere. The two collaborators first determined the temperature of inflammation of mixtures of hydrogen, methane, and carbon monoxide in various proportions with air, and found these to be lower than had been suspected. From this they passed to measurements of the velocity of propagation of flame, a subject on which research is even now being conducted. In the course of these studies, they found it necessary to determine certain physical constants for which, at the time, no figures were available. The only values of the specific heats of gases were those of Regnault, determined at atmospheric pressures and at temperatures not over 200°. Extrapolation of such values to high temperatures gave quite misleading results. By using Bunsen's method of explosion in a closed vessel provided with a pressure gauge, and so obtaining the temperature of combustion, the heat of combustion being determined calorimetrically, the specific heat could be calculated. Simple relations were found, including the practical equality of the molecular heats of the "perfect" gases (oxygen, nitrogen, hydrogen, and carbon monoxide) up to the highest temperatures, while increasing slowly with the temperature, and the effects of dissociation on other gases, such as chlorine, water vapour, and carbon dioxide. These data became of importance for the study of combustion in industrial furnaces as well as in their immediate application to explosions of mine gas, although certain sources of error were later discovered which necessitated numerical corrections in some instances.

In the course of these experiments it became evident that the means of estimating the quantity of fire-damp in the atmosphere of a mine were not sufficiently accurate, and the usual method of examining the change in appearance of the flame in a safety lamp was improved by using the non-luminous flame of alcohol in place of an oil or paraffin

flame. The apparatus for the analysis of mine gases was also simplified. Further, the same collaborators undertook a study of mining explosives, and succeeded in establishing general principles governing the choice of safe explosives, with results of considerable value to the mining industry.

The work on cements and that on gases at high temperatures had this in common that both investigations involved a study of chemical equilibria. Le Chatelier was never tired of expressing his indebtedness to Sainte-Claire Deville, and it was his studies of dissociation that brought home to him the importance of reversible reactions. The dissociation of calcium carbonate by heat, examined experimentally by Debray, is one of the primary reactions in the production of quicklime and of cement clinker. A study of the temperature of dissociation of this compound and of several others led him to consider the general problem of chemical and physical equilibrium. Le Chatelier's interest in thermodynamics, which led him to occupy a great part of his life in such studies, came in great measure from his sense of its importance for practice. As an example, he quotes the case of the blast-furnace reactions. The gross reaction may be expressed by the equation $Fe_2O_3 + 3CO = 2Fe + 3CO_2$, but the gas which leaves the furnace actually contains a considerable proportion of carbon monoxide. This was thought by some practical men to be due to insufficient contact between the ascending gases and the ore, and furnaces were in some places increased in height in order to obtain longer contact. No benefit was derived from the change, as was explained by Sir Lowthian Bell, and a knowledge of the laws of reversible equilibrium would have shown that the reversibility of the reactions made the presence of carbon monoxide inevitable. The knowledge actually existed at the time that the practical experiment was tried, but it had not been utilised by industry.

A note published in 1884 contains a generalisation of a principle enunciated by van 'tHoff for the effects of temperature only, extended to cover all variations of conditions. This, which is now known as the Le Chatelier principle, was at first rather cumbrously expressed. " Any system in stable chemical equilibrium, subjected to the influence of an external cause which tends to change either its temperature or its condensation (pressure, concentration, number of molecules in unit volume), either as a whole or in some of its parts, can only undergo such internal modifications as would, if produced alone, bring about a change of temperature or of condensation of opposite sign to that resulting from the external cause." This was the first of a series of papers on the laws of chemical equilibrium, summed up in a memoir of 126 pages in the *Annales des Mines* for 1888. The principle mentioned above is here stated in a form which is at once simpler and more comprehensive : " Every change of one of the factors of an equilibrium occasions a re-arrangement of the system in such a direction that the factor in question experiences a change in a sense opposite to the original change." Changes of electromotive force are included as well as those of pressure and temperature. The memoir contains a large number of applications of the principle, based on experiments which are partly original and partly taken from the work of others. Stress is laid on the empirical nature of the generalisation, but it has proved of great service in co-ordinating the facts of physical chemistry. Some later writers have even sought to represent the laws of biological and social evolution as special applications of this general principle.

While engaged in the preparation of this memoir, Le Chatelier met with the work of Willard Gibbs, and found that his main results had been anticipated, so far as their mathematical form was concerned. He considered, however, that the highly abstract presentation by Gibbs, having no reference to chemical data, could have been of little value to chemists. He was the means of presenting the work of Gibbs to the French public in a translation, and later of applying the doctrine of phases to solid systems in his studies of metallurgy. Much of this work was parallel with, but independent of, that of van 'tHoff, whom he frequently quoted in his later writings.

The same paper contains an interesting anticipation of later ideas. Le Chatelier succeeded in integrating the equations in which the free energy is expressed in terms of the heats of reaction and of the specific heats. The integration constant was, however, unknown, and the comment is made that " It is highly probable that the constant of

integration is a determinate function of certain physical properties of the substances in question. The determination of the nature of this function would lead to a complete knowledge of the laws of equilibrium. It would permit us to determine *a priori*, independently of any new experimental data, the full conditions of equilibrium corresponding to a given chemical reaction." It was further shown that if a chemical reaction is equivalent to the sum of two other reactions its constant of integration is the sum of their integration constants. Several other predictions followed, among them that for homogeneous gas reactions of similar character, such as that between hydrogen and the several halogens, the constants would be found to be nearly equal, as later experiments have shown them to be.

The *Annales des Mines* was not widely read by chemists, and these predictions appear to have been overlooked until the methods were revived by Nernst in 1909. Full justice was done to Le Chatelier by Nernst and by G. N. Lewis, but the work has passed unnoticed by many writers on physical chemistry. The teaching of such general ideas made slow progress in France, and as late as 1905 Henri Moissan refused to admit an article on chemical equilibria into his " Traité de Chimie Minérale," although Le Chatelier succeeded in, to use his own expression, " smuggling " six pages on the subject into his section dealing with cements.

True to his general principles, he sought to apply the knowledge gained in these studies to practical ends. One of the reversible reactions in blast furnaces is the decomposition of carbon monoxide into carbon dioxide and solid carbon, and under his direction this reaction was examined experimentally by O. Boudouard, resulting in the curve which is familiar to all metallurgists, the necessity of the presence of iron oxide as a catalyst if equilibrium is to be attained at the lower temperatures being also demonstrated. With another student, G. Chaudron, the equilibria between iron and its oxides, hydrogen, and water vapour were similarly determined. Although some of these data have since needed revision, they formed a model for later researches in this field. The work extended over many years. One such investigation calls for notice. The synthesis of ammonia from nitrogen and hydrogen presented special interest as a study in chemical equilibrium. That it would be of practical value seemed unlikely, as it was to be expected that the conditions would be difficult to realise. The fact that the union of the two gases is accompanied by a contraction showed that increased pressure would favour synthesis, whilst a catalyst would probably be essential. The notes of Thenard were at hand, in which it was stated that the dissociation of ammonia was complete at 600° in presence of metallic iron. This temperature was adopted, with a pressure of 200 atmospheres. The mixture of gases was forced by an air compressor into a steel Berthelot bomb, the reduced iron in the interior being heated by a platinum spiral. The result was an explosion which blew fragments of the heavy bomb through the floor and the ceiling. In the belief that combination of the gases had occurred, a patent was taken out as a means of securing priority. On examining the compressor later, however, it was found that a tap had been accidentally left open during the experiment, and that air as well as nitrogen and hydrogen had been forced into the bomb, thus accounting for the explosion. The work was abandoned, but the right conditions (of temperature, pressure, and catalyst) for the synthesis had in fact been attained in 1900, and both Haber and Claude acknowledged their indebtedness to this early record when they successfully achieved the industrial production of ammonia.

A paper published in 1906 indicates for the first time the method of drawing up the " thermal balance sheet " of an industrial furnace.

From 1883 onwards, Le Chatelier made a number of observations of polymorphic changes in solids. The first solid studied was boracite, and shortly afterwards, in collaboration with Mallard, he examined the dimorphism of silver iodide and the effect of pressure on the change, thus giving a further example of the principle which had been derived from the study of dissociation. The most interesting discovery, made by means of his modification of Fizeau's dilatometer, which could be used at temperatures up to 1000°, was the transformation of quartz at 570°. The other forms of silica were also studied, and the results were applied to the processes of manufacture of refractory materials and

to the examination of slags. A systematic work "La silice et les silicates," was published in 1914.

In 1887 he had exchanged his chair for that of Industrial Chemistry in the same College, and this post he retained until his retirement in 1919. In 1898 he succeeded Schutzenberger in the chair of Mineral Chemistry in the Collège de France, which he held for ten years, and in 1907 he succeeded Moissan at the Sorbonne. In these several teaching posts he had the opportunity of influencing a large number of students, and of introducing important reforms into the teaching of chemistry in Paris. Courses of lectures in inorganic chemistry had been largely catalogues of compounds, their preparation and properties. In Le Chatelier's lectures, the general principles of chemistry were taught and illustrated by concrete examples. The lectures were prepared with the utmost care, and the fine delivery of the speaker and the perfect clarity of his discourse made him an outstanding teacher. Widely read and with an excellent memory, he could advise his students as to their reading as well as guide their experimental work. His method may be seen in the volume published in 1908, "Leçons sur le carbone." This is described in the preface as the literal text of the lectures which he delivered at the Sorbonne in the session 1907—8. After a discussion of the meaning of science and of a scientific law, the work of his predecessor, Moissan, is related as illustrating the importance of studies of simple substances in a purely chemical manner. An account of the several forms of carbon and of their properties leads up to the subject of fuels. After a chapter on metallic carbides and their industrial importance, a survey of the oxides of carbon and the carbonates introduces the subject of the laws of chemical equilibrium, which are discussed on the lines of the author's previous work. A final section deals with the determination of atomic and molecular weights, but throughout the book, atomic conceptions are ignored, formulæ being used merely as a representation of combining proportions. The applications to industry are constantly introduced, and several of the chapters contain interesting sketches of the history of a discovery or of an idea. It is certain that the lectures made a great impression on their hearers, and left their mark on French chemistry. A somewhat similar treatment is found in "Le chauffage industriel," first published in 1912, and again reproducing a course of lectures. Starting from the general principles of combustion, the work treats of the nature of fuels and the determination of their value, passing to accounts of the production of gaseous fuels and the design of furnaces, stress being laid on principles rather than on technical details, which should, in the author's opinion, be learned in industrial practice.

The professor of metallurgy at the École des Mines, Lan, having become Director, invited Le Chatelier to undertake the lectures in that subject. He declined, on the ground that the field was quite strange to him, but he was persuaded to include a few lectures on metallurgy in his course on industrial chemistry. He gradually became more interested, and it is as a metallurgist that his name has been chiefly known to the later generation of scientific workers, his contributions to that branch of science having been numerous and outstanding. The accounts of metals, and especially of alloys, in chemical literature were unsatisfactory. Brilliant work on the structure of certain alloys had been done by isolated workers, especially by Sorby, but their investigations had been little noticed by chemists, who commonly looked on alloys as indefinite mixtures, somewhat resembling the glasses. As far back as 1863, Mathiessen had shown that alloys might be regarded as solidified solutions, but this idea had not been brought into relation with the phase rule or with other general principles, and such researches as those of Ramsay and of Heycock and Neville were little known in France. Le Chatelier undertook the improvement of methods of determining the temperatures at which alloys underwent changes on heating and cooling, employing thermal, dilatometric, and electrical resistance measurements for the purpose, and carrying these to higher temperatures than previous workers had used. In 1895 he pointed out that the study of the constitution of alloys comprised two distinct parts, (*a*) the chemical constitution, including the formation of intermetallic compounds and solid solutions and of allotropic modifications; and (*b*) the physical structure, or arrangement of the several kinds of crystal within the solid alloy. He showed that the widely used method of extraction with solvents and analysis of the residue

s a means of discovering definite chemical compounds between metals often led to misleading results, and that much more trustworthy information could be obtained by studying the variation of some physical property with composition and with treatment. The orm of the freezing point-composition curve, often presenting maxima at simple atomic atios, was particularly useful.

Sorby's method of polishing a flat surface of a metal and developing the structure by tching, and then examining it by reflected light, was taken up by Floris Osmond, then ngaged in the steel works at Le Creusot, whose first paper on steel was published in 1885. )smond discovered the allotropic changes in iron, and explained the hardness of quenched teels by the retention of a hard variety of iron, stable at high temperatures, on rapid ooling. Osmond's method of preparation of the specimens was cumbrous, more so than hat of Sorby twenty-five years earlier, and Le Chatelier, wishing to learn his technique, ucceeded in making a number of improvements, including the use of alumina, prepared y igniting ammonium alum, as a polishing powder in place of rouge. The consultations etween these two workers led to a clarification of their ideas, and Le Chatelier's paper in he *Revue générale des Sciences* in 1897 placed the whole subject of the hardening of steel n a new light. The laminated structure discovered by Sorby and known as pearlite was oticed to be very similar to that of a eutectic, and was to be regarded as formed by the reaking up of a solid solution, stable at high temperatures, into two phases, in this instance ron and iron carbide (ferrite and cementite), a process quite parallel with the simultaneous crystallisation of two phases from a liquid solution. Quenching suppressed this esolution of the solid solution, but not the allotropic change in the iron, so that the hard onstituent, known as martensite, was to be considered as a solid solution of carbon in he low-temperature modification of iron ($\alpha$-iron). The behaviour of certain alloys of iron vith nickel and with manganese, which were not hardened by quenching, was used to onfirm this view, the high-temperature, non-magnetic form of iron being preserved in hem unchanged. The idea of an intrinsically hard modification of iron ($\beta$-iron) was nly slowly abandoned by some metallurgists, and controversy continued for many years, ut the essentials of the modern view are to be found in the paper of 1897. In 1899 Roberts-Austen published the first freezing-point curve of the iron-carbon system, noting t the same time many of the thermal arrests at lower temperatures. These data, which Le Chatelier's paper made it possible to interpret, were used by Bakhuis Roozeboom to onstruct the first equilibrium diagram for the series, which, although since modified in nany respects, has the general form of the diagram used to-day, the form of the curves aving been determined with great care by Carpenter and Keeling in 1904, and since nodified in detail by many workers. The paper by Roozeboom, the first application of he phase rule in detail to a metallic system, gave a new impetus to the study of the netallography of steel, and thence to that of alloys in general. A committee was formed n France, at the instigation of Le Chatelier, and in 1901 a volume appeared, "Contribution à l'étude des alliages," containing papers by the leading French metallurgists, and this, in he absence of formal text-books, was long used as a work of reference. It contained important papers by Osmond, Charpy, and others, and reprinted several contributions of Le Chatelier. These described the methods of investigating the constitution of alloys by letermining their physical properties, with the aid of improved instruments which he had levised for the purpose. The most interesting of these was an improved form of microscope, designed specially for work with metals. Hitherto, microscopes of the biological ype had been used, with the addition of devices for illuminating opaque objects by vertical or inclined rays. Although the photo-micrographs of the copper-tin alloys, made at this time by Heycock and Neville, which have hardly been surpassed by later workers, were made with such a microscope of the simplest type, most investigators had much difficulty in placing the specimens under the best conditions for illumination, the levelling on the stage being particularly troublesome. Le Chatelier departed entirely from the ordinary construction, and placed the specimen face downwards, without mounting, over the opening of a stage, the objective being below, and the direction of the rays changed by means of prisms. This inverted instrument proved to be exceedingly convenient in practice, and the principle was later adopted by most makers of metallographic micro-

scopes, including the most elaborate of modern instruments. It has the disadvantage of adding to the number of reflections, and for this reason some makers are reverting to the older type, taking advantage of improved methods of lighting, but most photographic work is done with the inverted form of instrument.

He made several minor improvements in metallographic technique, as in the preparation of polishing powders of regulated fineness and in the use of electrolytic methods of etching.

With increasing teaching responsibilities, Le Chatelier's experimental work naturally became more restricted, but he continued to supervise the work of students, and frequently published notes on metallurgical questions. In order that French metallurgy might have an organ of its own, he founded in 1904 the *Revue de Métallurgie*, having the support of the Société d'Encouragement and of the Comité des Forges in the undertaking. The new journal, under his active direction, at once took a leading place, which it has since retained. One paper, contained in the first volume, may be mentioned, as it represented an attempt to study the effect of different cooling liquids on the quenching of steel, cooling curves being taken by means of a thermocouple attached to the specimen. The spot of light from the galvanometer was received on a moving plate, a pendulum being arranged to interrupt the beam every second to facilitate counting. The galvanometer, of very low resistance, was not sensitive enough for high accuracy, and Le Chatelier pointed out that for a more refined study a thread galvanometer or an oscillograph should be used. This was actually done by later workers, and in the hands of German metallographers the method has been developed in a remarkable way, so as to include exceedingly high rates of cooling, but the pioneer work constituted a valuable step.

An article in the *Revue de Métallurgie* on the high-speed tool steels developed in America by F. W. Taylor and his collaborators led to a correspondence with Taylor, who wrote that since completing the investigation he had devoted himself to a larger problem, that of the organisation of factories. Le Chatelier became a fervent advocate of Taylor's principles, which were fully in accordance with his own ideas of the need for introducing scientific method into the conduct of industry. In his view, Taylor's methods consisted essentially in planning a technical operation by the study of each of the factors concerned in it, human as well as mechanical, as one would plan the determination of the velocity constant of a chemical reaction. The details of the system as applied to a factory have been much criticised, but the plan of setting apart a special staff for the planning of the operations required for a given product has proved its value, however difficult the application may be in a given case. Le Chatelier returned again and again to the subject, and collected several of his memoirs, with a new preface, in a volume entitled "Le taylorisme," first published in 1928.

The European war brought new duties. Routine teaching was suspended for a time, and Le Chatelier turned to matters connected with national defence, including an important metallurgical problem, the heat treatment of shells. After the close of the war, he continued his work of writing and of pressing forward the reform of the teaching of science and of the conduct of those industries which depend for their success on the application of scientific knowledge, while returning from time to time to the special problems of metallurgy in which he had so long been interested. In 1925 he published a little volume, "Science et industrie," and in 1936, only a short time before his death, this was revised so as to represent his considered opinion in the light of later experience, and re-issued under the title "De la méthode dans les sciences expérimentales." After reviewing the general principles of science, and making use of the classical essay of Descartes, he discusses methods of observation and the way in which discoveries are made, passing on to questions of apparatus and of experimental errors. His illustrations are largely drawn from his own work or from that of such teachers and friends as Deville and Osmond. The later chapters deal with plans of teaching, especially of chemistry and technology, with the application of science to industry, and with the Taylor system.

This small work throws an interesting light on the attitude of its author towards science. Laying stress on the need for accurate observation and experiment, he constantly warns against the misuse of hypotheses. Recognising fully the need of working

ypotheses as a means of progress, he insists on the possibility of experimental verification ; a test of their value, and regards those which are not accessible to experiment as ex-edingly dangerous. In his own work, he avoided as far as possible even the conception atoms, using formulæ as expressions of chemical composition merely. His work was onfined to inorganic chemistry, so that he never had to concern himself with questions structure, which would inevitably have called for atomic conceptions, but it is instructive o follow his work, and to observe how independent the results obtained are of any ideas f the constitution of matter. For modern physical theories of the atom he had no taste, nd he became more conservative with advancing age. For the inorganic chemist, how-ver, at a time when students are often encouraged to build up their knowledge of chemistry n a basis of theories of the structure of the atom, there are lessons to be learned from uch a purely chemical treatment of the reactions between substances, including the uantitative thermodynamical study of chemical change. There is much that is sug-estive in these chapters, and the author's aim of bringing together pure and applied cience is clearly brought out. He shows how chemistry arose from the practical needs f mankind, and how the constant reciprocal action of pure science and industry has elped and stimulated both. This thesis is illustrated by a wealth of examples, almost ntirely French. One of the objects of the book, indeed, is to insist on the supremacy f French science, although he holds, somewhat unexpectedly, that French industrialists ave lagged behind other countries in the application of the discoveries of their com-atriots. His teaching and influence, exerted especially during the years following his fficial retirement, must have done much to remedy this. His zeal for the advancement f industry was quite disinterested, as he never sought monetary reward. Intensely atriotic Frenchman as he was, he had many friends in other countries, some of whom ad worked in his laboratory, whilst others had made his acquaintance through his writ-ngs. The memorial issue of the *Revue de Métallurgie* contains eloquent tributes from metal-urgists of many countries, which are sufficient evidence of the respect and esteem in which e was held. He was a familiar and welcome figure at international congresses, to which e often contributed.

Le Chatelier received many honours in the course of his long life. He was admitted o the Académie des Sciences in 1907, succeeding Henry Moissan. He became a Foreign Member of the Royal Society in 1913, received the Davy Medal in 1916, and was elected Foreign Member of our own Society in 1908. The Iron and Steel Institute awarded im the Bessemer Medal in 1910, and he received honorary doctorates from Aachen, Manchester, Copenhagen, Louvain and Madrid. In 1922 his scientific jubilee was cele-rated at the Sorbonne, a medal being struck in his honour, and a small volume was sued, containing the addresses delivered on that occasion. As late as October 1936, as Honorary President, he gave an eloquent address to the International Congress of Mines, Metallurgy and Geology in Paris, receiving an enthusiastic welcome. His health was xcellent, but deafness troubled him in his later years, although he kept up his personal iendships to the last. When well over 80 he travelled to Morocco. His death came on he 17th September, 1936, at Miribel-les-Échelles (Isère). Only three days before, when he Institute of Metals was meeting in Paris, a cordial letter of greeting from him was ead, but when the meeting of the Iron and Steel Institute opened a few days later in Düsseldorf, the news of his death was the first announcement made by the chairman.

Henry Le Chatelier married, in 1876, Mlle. Geneviève Nicolas, and their descendants omprised seven children, thirty-four grandchildren, and six great-grandchildren. A amily photograph taken on the occasion of the sixtieth anniversary of his wedding includes orty-four persons. His widow and many of his family were present at the commemoration t the Sorbonne on 24th April, 1937, presided over by the President of the Republic, M. Albert Lebrun, who as a mining engineer had been one of his students and spoke in is address of the impressions produced by his teaching. Addresses were given by repre-entatives of the several branches of chemistry and industry with which he had been ssociated, and Prof. Carl Benedicks spoke on behalf of the many representatives of oreign societies present.

All who knew Le Chatelier recognised his high character and lofty ideals. Anxious

as he was for the progress of industry and for the improvement of material conditions, he had always in mind the moral as well as the material welfare of mankind. In the address to the Mining Congress already referred to, after an eloquent passage on the relations of science and morals, he added :

> " Let us hope, without deceiving ourselves too much, that if the 19th century remains celebrated in the records of humanity for the progress of the experimental sciences and for the creation of industry on the large scale, the 20th may distinguish itself by its understanding of social problems and by its love of justice,"

and in an article which he was revising on the day of his death, he urged that the vital problems of industry to-day are essentially moral problems. This conclusion is consistent with the whole of his life work. With Latin clarity of thought, and in the best traditions of French philosophy, he looked on human thought and activity as a whole, and in his interest in special problems never lost sight of their bearing on human welfare.

I am indebted for much information to the memorial number of the *Revue de Métallurgie,* and especially to the article by Prof. Léon Guillet. M. François Le Chatelier, of Ugine (Savoie), has kindly supplied me with further notes about his father's work, and with the excellent photograph, taken a few years ago by M. Louis Lumière. A survey of Le Chatelier's work on thermodynamics and chemical equilibria is contained in the full obituary notice by Prof. P. Pascal (*Bull. Soc. chim.*, October, 1937).

# OBITUARY NOTICES.

## OTTILIE BLUM-BERGMANN.

1900—1937.

OTTILIE BLUM-BERGMANN received her early chemical training in Vienna under the direction of Professor Schlenk, and completed her thesis there on "The Structure Of Indophenine." In 1921 she proceeded, together with Professor Schlenk, to Berlin University, where she worked as his assistant until, in 1933, owing to the political situation in Germany, she was compelled to leave the country. After a few months' stay in London she accepted a position in the Daniel Sieff Research Institute, Rehovoth, Palestine, where she continued her scientific work in collaboration with her husband, Dr. Ernst Bergmann, until her death, which occurred on May 16th, 1937, in her thirty-seventh year.

Her work in Berlin was concerned mainly with the chemistry of the alkali organic compounds, and stereochemical questions, according to the general trend of work in Professor Schlenk's laboratory. Later she turned her attention to the chemistry and synthesis of aromatic compounds allied to the steroids. She explored the possibilities of building up the indene system which is one of the fundamental features in the molecular structure of these cyclic compounds, and she applied the experience so gained to the actual synthesis of representatives of this group. She showed that some of her products had oestrogenic properties, which, at that time, was uncommon with synthetic compounds.

Of her recent work, the synthesis of methylcholanthrene, *cyclo*pentenotriphenylene and 2 : 3-*cyclo*pentenophenanthrene may be mentioned. Following the tradition of Professor Schlenk and his co-workers, she remained always interested in theoretical problems and at the time of her death had just completed two papers on the mechanism of the Wurtz–Fittig reaction and the addition of ketens to ethylenic bonds.

HAROLD DAVIES.

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## MAY SYBIL BURR.

1887—1937.

MAY SYBIL BURR (née Leslie) was born on August 14th, 1887, at Woodlesford (W.R., Yorks). Her scientific bent was clearly indicated when she graduated with First Class Honours in Chemistry at Leeds in 1908. In the following year she was elected to an 1851 Exhibition Science Scholarship and proceeded to Madame Curie's laboratory at the Sorbonne, where for two years she worked on problems connected with the radioactivity of thorium and its disintegration products. Renewal of the scholarship for a third year permitted her to spend some time with Rutherford at Manchester.

Her teaching career began with a post as science mistress at the Girls' High School, West Hartlepool, and this was followed by experience as Assistant-Lecturer in Chemistry at University College, Bangor.

From 1915 to 1918 she acted as chemist-in-charge of laboratories in H.M. factories concerned with the manufacture of high explosives at Litherland (Liverpool) and Penrhyndeudraeth (N. Wales) and in this capacity contributed effectively towards the solution of urgent technical problems.

She returned to Leeds in 1918 as Assistant-Lecturer in Inorganic Chemistry and was subsequently transferred to the Department of Physical Chemistry, where she took an important share of the teaching work both as lecturer and as assistant in charge of the laboratory.

In 1923 she married Mr. A. H. Burr, Lecturer in Chemistry at the Royal Technical College, Salford, and later moved to Scotland, where her husband became Head of the Chemistry Department at Coatbridge Technical College. On his decease in 1933 she took up the investigation of various kinetic problems and was thus engaged until a month prior to her death, which occurred on July 3rd, 1937.

Mrs. Burr's reputation as a scientific worker was deservedly high; on the list of women graduates of the University of Leeds her name is the only one distinguished by the award of the D.Sc. degree. In addition to her published original work, she wrote the section on the alkaline-earth metals in Friend's well-known "Text Book of Inorganic Chemistry," and (in collaboration with J. C. Gregory) the section on beryllium and its congeners.

As a teacher she was exceptionally gifted and spared no effort to remove the difficulties encountered by students in their contact with scientific problems whether of chemical, physical, or mathematical nature.

Her aptitude was, however, by no means confined to science and it may be recalled that her contact as an undergraduate with the Department of English Literature led to the expert opinion that she would most certainly achieve distinction in the Faculty of Arts if she cared to forsake the study of chemistry.

To her intimate friends she was known as a woman of the highest ideals, of wide human sympathies and of great earnestness of purpose. Her reticence and innate modesty limited the circle of her acquaintances, but such restriction would doubtless count for very little in comparison with the respect and sincere regard of those who were privileged to enjoy her confidence.

H. M. Dawson.

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## JOSEPH BERNARD COLEMAN.

### 1859—1937.

Coleman was born at Arnold, Nottinghamshire, in 1859, and died at his residence in Norwich on July 11th, 1937. His name is well known in the world of analytical chemistry, largely on account of the books on this subject of which he was co-author. In 1879 he took up a Royal Exhibition at the Royal College of Science, Dublin, and after a brilliant career as a student he obtained the Diploma with first place on the examination list. In 1892 he was appointed to University College, Nottingham, ultimately becoming Senior Demonstrator and Lecturer in Pure and Applied Chemistry. Here he became associated with the late Dr. Clowes, an association which continued actively up to the time of his colleague's death in 1923. He was elected a Fellow of the Institute of Chemistry in 1887 and he was a member of the Society of Chemical Industry. In 1895 he came to the South Western Polytechnic Institute, Chelsea, as the first Head of the Chemical Department, and remained at this post up to the time of his retirement in 1924. His work and interests centred principally round the teaching of analytical chemistry. He was a finished analyst, and a clear teacher. During his work with Clowes, they conceived the idea of writing a practical book on quantitative analysis which should embody their experience of teaching the subject, and should serve to smooth the somewhat thorny path of the average chemical student of those days. The book was first published in 1891, and was an immediate success. It has run through thirteen editions. A shorter volume on the same lines was published in 1891. He collaborated in several other books on practical chemistry, qualitative analysis, and practical agricultural chemistry. These works were under constant revision. He did not believe in resting on his oars, and the results are seen in the continued popularity of most of these works. In his early days at Nottingham, he was Assistant Consulting Chemist to the borough from 1887–1894. During the war he was engaged in the work of collecting matter for the Chemical Information Committee on Lubricants, of which he was Chairman, for the Department of Scientific and Industrial Research.

It will be gathered that these activities, combined with his teaching and departmental organisation, left him little leisure for research. His published papers and articles deal with analytical methods and laboratory equipment.

Coleman was a man of outstanding personality and indomitable will, an able organiser, withal attractive and of a cheerful temperament. He was always ready to consider suggestions, which were, however, subjected to critical examination. He was very careful to satisfy himself of the reliability of any matter included in the books written with his co-authors. His insistence on correct experimental procedure, his sense of justice, and his

keen interest in the students themselves, and in their social and athletic activities have left his impress on hundreds of his old students now working in all parts of the world.

J. C. Crocker.

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## JOSEPH COWPER.

### 1866—1937.

Joseph Cowper, who died on November 28th, 1937, was born in Penrith on January 16th, 1866. Leaving Mr. James Briggs' school at Sockbridge House in that town at an early age, Cowper was apprenticed to Mr. Redfern, of King Street, and became a qualified chemist and druggist at 21 years of age, and for two years managed a business for the late Mr. Senier at Norwood. He then returned to Penrith and became proprietor of the business where he served his apprenticeship. Under his able guidance the business grew rapidly and in 1899 was converted into a limited liability company, of which he was Chairman until, in 1921, at a comparatively early age, he decided to retire. Apart from long and constant association with the Tradesmen's Association, Cowper took little part in local affairs. He was, however, a prominent Freemason and a keen collector of antiques, upon which he was a recognised authority.

He was elected a Fellow of the Society in April, 1888.

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## FREDERICK JONATHAN DOWN.

### 1855—1937.

F. J. Down, who died at his home at Harpenden, Hertfordshire, on October 17th, 1937, aged 82 years, was born in Cheshire in 1855. He joined the Society in November, 1884, attaining his jubilee as a Fellow in 1934. As a young man, Down read chemistry and studied in Germany under Fresenius, afterwards taking an appointment with the Blaydon Manure and Alkali Company Ltd. Later, he was attracted to electrical engineering, particularly electric lighting, and secured the representation of the American Thomson-Houston arc lighting system for Great Britain. He became a partner in the firm of Laing, Wharton, and Down, which carried out much pioneering work in the extension of the use of electricity for all forms of lighting and power and from which the British Thomson-Houston Company developed. He took an active share in forming the Overhead Lines Association and in recent years his business was concerned with the provision of appliances for the construction of systems for overhead distribution of current.

Down was a man of untiring energy and genial personality. He carried on his work almost to the last, and he will be greatly missed by a large circle of business associates as well as by his many personal friends.

C. T. Gimingham.

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## CHRISTOPHER MAURICE WALTER GRIEB.

### 1885—1937.

C. M. W. Grieb died at Munich on July 14th, 1937, in his 53rd year as the result of a motor accident while spending his summer holiday in Bavaria.

On leaving school Grieb proceeded to University College, London, where he studied under Sir William Ramsay and Professor J. Norman Collie, obtaining his B.Sc. (Hons.) at the end of the three years' course. After a further year spent in carrying out research with Ramsay, Grieb was appointed Analytical Works Chemist to Messrs. Lorimer and Co., Manufacturing Chemists and Druggists at Islington. In 1909, he became Chief Chemist to Messrs. R. Fry and Co., Mineral Water Manufacturers at Brighton, and after a short stay there, entered the services of Nobels Explosives Co. at Polmont as Chief Laboratory Chemist, becoming after four years Works Manager at their filling factory at Perranporth, Cornwall.

In 1919, he was appointed Chief Chemist to the Mond Nickel Co. at Clydach. Here he was in charge of the experimental and research work in connection with all processes and plant. He specialised in the analysis of precious metals and their recovery from ores and residues and in the manufacture of liquid nickel and iron carbonyl. In conjunction with R. H. Jones, he published a paper entitled " Phosphides of Nickel : The Reaction between Phosphorus and Nickel Carbonyl " in the *Journal* for 1932.

Possessed of an even temper, patience and persistence, Grieb was very conscientious in all his work, and was a good linguist. He took a prominent part in the social life of the Works, and in particular with the Carbonyl Dramatic Society and the Works Orchestra. He acted as Chairman of the South Wales Section of the Institute of Chemistry from 1926 to 1928, and of the South Wales Section of the Society of Chemical Industry in 1934. He was elected a Fellow of the Chemical Society in February, 1907.

He is survived by his widow and two sons.

EMILE MOND.

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## ROBERT OSWALD HALL.

### 1905—1937.

ROBERT OSWALD HALL died suddenly (the result of an accident) on November 28th, 1937.

He was born on June 24th, 1905, and educated at Wakefield Grammar School from 1916 to 1923. In 1924, he entered Leeds University, where he took the Honours Chemistry course, holding the Lord Kitchener National Memorial Scholarship from 1925 to 1929. In 1927, he gained 2nd Class Honours in the degree examination, becoming a B.Sc., and was also granted the Walker-Wilson and Clothworkers' Research Scholarships in Textiles.

During the following three years, Hall took part in a general study of the hygienic properties of clothing, and investigated the laws governing the transmission of water vapour through textile fabrics as a function of their structure and the nature of the component fibres. An account of the work is to be found in the thesis on " The Ventilating Properties of Textile Materials and Fabrics," for which he was awarded the degree of Ph.D. at Leeds University in 1930. The same year, he was elected an Associate of the Institute of Chemistry, and was appointed an Assistant Chemist in the Government Laboratory, Clement's Inn.

In February, 1931, Hall was appointed Research Fellow of the Textile Department, Ontario Research Foundation, Toronto, where he remained for three years. Here he carried on a series of investigations relating to the quality and specifications of textile materials as used in the motor-car industry. This work led him into a number of separate lines of research of a fundamental character. Thus, in regard to the colour of fabrics, he devised an instrument by which it was possible to determine the fugitivity of dyes, nnder controlled conditions of temperature and moisture, but under intense illumination, which greatly accelerated the fading. He was appointed to draw up standards of fastness acceptable to the two branches of industry concerned. Other aspects of his work were concerned with standards of length measurement in relation to the atmospheric humidity and hence the moisture content of textile materials. In addition to such problems as these, which were undertaken on account of their immediate importance to industry, he found time to pursue enquiries of a more academic character, particularly an investigation of the absorptive behaviour of the wool fibre in relation to the degree of swelling.

Early in 1934, Hall accepted an offer of the position of Research Chemist with Messrs. C. W. Martin & Sons, Ltd., Bermondsey, S.E.I., in connection with their processes in dressing and dyeing furskins. During the past three years, he carried out fundamental research on the behaviour, under different conditions, of the individual fibres constituting the fur and pelt of skins. For these investigations he worked out a special technique in microscopy which led to some extremely novel and interesting results. Other problems investigated by him included " singeing " of hairs, bleaching of ermine, and unhairing of fur seals. His abilities as a physicist proved of great value in work connected with the conditioning and drying of skins.

Hall represented the best type of scientist, logical, clear-thinking and of wide experience; by reason of these qualities his views commanded respect and attention. In addition to his extensive activities in industrial research work, he was a keen sportsman and athlete and obtained his colours at Leeds University for boxing. He represented the University at the inter-varsity boxing competitions in London and Manchester, and was also a prominent member of the University team of harriers, taking part in many of their cross-country events.

His loss will be felt not only by scientific workers who had come in touch with him, but by his colleagues and friends who were attracted by his cheerful disposition and sound judgment. He leaves a widow and one child.

Hall was elected a Fellow of the Society in February, 1937.

R. E. Garrod.

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## SIR HERBERT JACKSON.*

### 1863—1936.

Emeritus Professor Sir Herbert Jackson, K.B.E., F.R.S., was born at Hampstead on March 17th, 1863. From King's College School he entered King's College, London, in 1879 and worked as student. Daniell Scholar, and Student-Demonstrator under Professor C. L. Bloxam until the latter's retirement in 1887, much of his work being carried out in Professor Bloxam's private laboratory. He was appointed Lecturer in Chemistry shortly after John Millar Thomson had succeeded Bloxam, became Assistant Professor in 1902, and Professor of Organic Chemistry in 1905. In 1907 he was elected a Fellow of King's College and on the retirement of Thomson in 1914 was appointed Daniell Professor of Chemistry. He resigned from this position in 1918, with the title of Emeritus Professor, on his appointment as Director of Research of the British Scientific Instrument Research Association.

During the whole of his 39 years at King's College Jackson associated himself closely with the various athletic and social activities of the College, making contact with and gaining the affectionate regard of the students of all faculties. Among the students in Science and Engineering, and particularly among the students specialising in Chemistry, he earned the reputation of being an inspiring teacher and an attractive lecturer, while his skill as an experimenter, his fertile imagination, and his versatility were recognized by all who had any close contact with him or intimate knowledge of his work.

Having regard to the large number of investigations in which Jackson interested himself while at King's College, his publications were remarkably few. About 1890 he began work on the production of fluorescent and phosphorescent materials, and made a considerable study of the behaviour of such materials when excited by ultra-violet light or by exposure to the electric discharge in low-vacuum and high-vacuum discharge tubes. The discharge tubes which he used were constructed throughout by himself, and he produced a number of types for the purpose of investigating how the brightness and distribution of the phosphorescent effects obtained could be modified by changing the form of the glass envelope, by fitting electrodes of different shapes, and by altering the disposition of the electrodes. In the course of this work he discovered that in high-vacuum tubes fitted with concave cathodes, the response of the phosphorescent material used as the anti-cathode could be restricted to a comparatively small area at or near the centre of curvature of the cathode, and that, in some cases, the phosphorescent material became considerably heated in this area. He also used tubes fitted with anti-cathodes made of non-phosphorescent materials, including metals, to investigate the possibility that such materials might emit invisible phosphorescent radiations when excited in an electric discharge tube. To detect any ultra-violet radiation which, originating at the cathode, might be transmitted through the glass walls of the tube, he used screens of phosphorescent materials held close to the tube and in some cases observed that the screens glowed visibly.

* Reprinted by permission from the *Proceedings* of the Royal Society.

His interest throughout this work was in the phosphorescent effects rather than in the mechanism by which they were produced. His views regarding that mechanism, stated many years later in conversation, were that the electric discharge caused the cathode to emit ultra-violet radiation which, falling on the anti-cathode, excited the phosphorescent response on the anti-cathode material. The glow of phosphorescent material held outside the tube was considered to be a "secondary" phosphorescence excited by ultra-violet radiations present in the "primary" phosphorescent emission from the anti-cathode. The fact that radiations emitted by the anti-cathode could penetrate the glass walls of the tube, and could excite a screen held outside the tube, was taken to indicate that the wave-length of the radiation emitted by the anti-cathode was not shorter than 3000 A.

There can be no doubt that the response of the phosphorescent screens held close to the tube was, in some cases at any rate, due to *X*-rays emitted by the anti-cathode and that, had the observations been viewed from a different standpoint, Röntgen's discovery might have been considerably anticipated. At no time, however, did Sir Herbert Jackson advance any claim to be the original discoverer of *X*-rays, or countenance any suggestion that such a claim might be made on his behalf. Throughout these investigations he had considered that he was dealing with comparatively long-wave ultra-violet radiations and he expressly stated on several occasions that the characteristic penetrating power of the radiations emitted by the anti-cathode was neither discovered nor suspected by him.

In a paper read on March 5th, 1896 (Proc., **12**, 57) Jackson described a discharge tube, fitted with a concave aluminium cathode and an inclined platinum anode, which he had made and used during January, 1894, and with which, or with a replica, he had been able to reproduce all the effects described in Röntgen's original announcement made in December, 1895. This tube, the original Jackson "focus-tube," was used in May, 1896, for a demonstration of *X*-rays at a Conversazione held at the Royal Society; its main features were subsequently adopted universally for the construction of all "gas" *X*-ray tubes.

In 1898 he gave a discourse on phosphorescence before the British Association at Bristol, and in 1900 he dealt with the same subject in a series of juvenile lectures at the Royal Society of Arts.

Jackson's other scientific activities between 1890 and 1914 were numerous and diverse in character and are very inadequately represented by those described in any published records. He made an extensive study of the weathering of stones in Westminster Abbey, Canterbury Cathedral, and other public buildings, and carried out a considerable amount of work in the experimental treatment of stones to prevent or retard decay due to weathering action. He also interested himself in problems connected with laundry-work, investigating the action of alkalis, soaps, oils and chemical solvents on fabrics of various types, and as detergents for the cleansing of fabrics soiled in different ways. This work formed the basis of the lectures and practical course given to special classes arranged at King's College, which were attended by launderers from a wide area. The practical value of the course-work and of the advice which Jackson was able to give on problems submitted to him by those attending the classes was highly appreciated, and the importance of the step which he took when he put his chemical knowledge so effectively at the service of the laundry industry has been increasingly recognised. His investigation on the action of detergent and bleaching agents was later described in two series of Cantor Lectures given before the Royal Society of Arts in 1907.

Published papers describing his investigations included a joint paper with D. Northall Laurie, contributed to the Chemical Society in 1905, relating to the reactions of carbon monoxide on ammonia. Further joint papers with Laurie, "On the Behaviour of Vapours of Methyl Alcohol and Acetaldehyde with Electric Discharges of High Frequency," and "On the Behaviour of Acetylene with Electric Discharges of High Frequency," were contributed to the Chemical Society in 1906. He also gave, in the same year, a course of juvenile lectures on Combustion and Flame at the Royal Society of Arts. An investigation carried out in collaboration with Professor Bottomley, on the growth of plants in atmospheres devoid of carbon dioxide but containing various proportions (1—70%) of carbon monoxide, was described in the *Proceedings* of the Royal Society (1904, **72**, 130).

In this investigation it was found that green plants could grow in such atmospheres and that starch was formed in the plants during their growth.

Of his other work in pure chemistry there appears to be no written or published record, and he seems to have relied almost entirely on his memory to keep track of the investigations which he carried out. The extent and variety of those investigations could be estimated from the collection of preparations, labelled in his own handwriting, which he preserved for many years and, to some extent, from his note-books. Most of his note-books contained schemes of investigation drawn up in considerable detail, followed by notes on a few preliminary experiments but, apart from an occasional note or formula jotted down later, gave no indication of the extent to which the investigation had been pursued or of the results which had been obtained in the later stages. From such records as he preserved, it is clear that he paid attention to the production and collection of vapours and gases, including rare gases, in a high state of purity, to a study of colloidal suspensions and of their behaviour in the presence of alkalis, salts, and acids, to the devising of sensitive tests for various poisons, and to methods of separating metals having closely similar chemical properties such as neodymium and praseodymium. But although some idea of the work which Jackson carried out could be obtained from his specimens and preparations, and from such notes as he had kept, the best evidence of its extent and variety was, undoubtedly, the wealth of information which he could bring to bear on almost any problem brought to his attention, and his insight into the fundamental chemical relations underlying the many problems on which he was asked for an opinion.

Many chemical problems encountered in industrial practice were also handled by him while he was at King's College, although, on account of the confidential character of most of this work, it was little known. It included such things as a study of methods of promoting crystallisation of solids by heating them in the presence of various salts, problems relating to the dispersion of clays in colloidal suspension, the production and testing of refractories, and many others. His interest in the chemical reactions which occur between solids at high temperatures and with the associated changes of physical structure was later extended to a study of pottery and porcelain in general, and was the foundation of his work on Chinese and other Oriental ceramics.

He also worked on problems encountered in the manufacture of gun-cotton and suggested modifications in the manufacturing processes with a view to retarding deterioration such as might lead to spontaneous ignition of the gun-cotton when kept in store.

Outside his purely chemical work and his work on phosphorescence, Sir Herbert Jackson's activities extended to any subject involving chemical processes and to any form of instrument or apparatus which might be of use in chemical investigations. In the early days of "wet plate" photography he experimented on the preparation and sensitising of emulsions and on methods of developing plates coated with the various experimental emulsions which he produced. Later he investigated the action of many reducing agents with a view to their use as photographic developers and produced special developers for ordinary plates and for plates to be used in colour photography. He also worked out a variety of unusual toning baths for photographic prints and experimented, in fact, on every chemical process involved in photographic technique. He invariably acted as demonstrator at the many public lectures on photography given by J. M. Thomson, and his dexterity in photographic manipulative processes of all kinds contributed greatly to the effectiveness and success of those lectures. Jackson's interest in photography was not, however, confined to the chemistry of photographic processes. He was an enthusiastic but discriminating amateur photographer with a good eye for "composition," as is shown by the subjects which he selected for his stereoscopic photographs and for photography in colour, as well as by his large collection of prints and lantern slides.

The use of the spectroscope in chemical analysis was another subject to which Sir Herbert Jackson paid considerable attention, mainly in connexion with the detection and identification of minute amounts of inorganic materials present as colouring agents or as impurities in drugs, glasses, metals, salts, etc., or introduced during manufacture into papers, fabrics, dressed leathers and similar materials.

Optical instruments of all kinds appealed strongly to Sir Herbert Jackson but the

instrument which he used more than any other was the microscope. He had made extensive use of the microscope throughout his scientific work for the examination of his various preparations and to follow out the effects produced by heat and other treatment on clays, porcelains, fibres, etc.

In addition he had interested himself in all the more usual types of microscope objects, in the technicalities of microscopy, and in the instrument itself. As a result he was adept in the adjustment and use of the microscope and its accessory apparatus, and familiar with the appearances of an extraordinarily wide variety of objects under the microscope when illuminated in different ways. He was also well acquainted with the diffraction effects produced by minute structures and with the way in which such effects could be varied by altering the conditions of illumination under which the structures were examined. His translation of what he saw under the microscope was invariably sound but the value of his work with the microscope was enormously enhanced by the fact that he could consider his observations in the light of his extensive chemical and other scientific knowledge. His deductions drawn from the microscopic examination of some fragment or specimen often indicated a line of investigation which gave an almost immediate solution of the problem in hand whether that problem related to the nature of the fragment or specimen, to the method by which it was produced, or to the nature and cause of corrosion or other form of deterioration which the fragment or specimen had suffered.

Jackson was always ready to put his knowledge of the microscope at the disposal of others, and he would at any time undertake either the complete examination of a specimen referred to him for his opinion or would demonstrate how the examination could best be carried out; it was a privilege and a pleasure to work with him on such occasions and to be allowed to benefit by his experience. He regarded his microscopes and microscopic equipment with a very real affection, and the enthusiasm with which he threw himself into every subject in which he became interested was exemplified in its extreme form in his microscope work.

During the first few months of the Great War Jackson's advice was sought on a variety of problems including the production of toluene, the manufacture of certain drugs, and work connected with the Censor's Office. He served on many of the Committees dealing with the production and supply of essential war-materials, but the outstanding feature of his war-time activities was his work on glass. This was undertaken, in the first place, for the Research Committee of the Institute of Chemistry, and in a very few months be developed batch mixtures for some ten varieties of glass, the formulæ for which were published in the *Journal of the Institute of Chemistry*, April, 1915. These included ordinary soda-glasses for laboratory glass-ware and for *X*-ray tubes, and a number of special glasses, such as combustion-tube glass, a chemically inactive glass for ampoules, miners' lamp glass, and others.

Later, for the Ministry of Munitions, he undertook the development of formulæ for a wide variety of optical glasses, and he also worked out batch mixtures for thermometer glasses, opal-backings for thermometers, glasses for artificial eyes, vitrite for the capping of electric lamps, and a special heat-resisting glass comparable in properties and composition with the "Pyrex" glass which was prodnced commercially several years later.

Most of this work on glasses was done during the evenings in a small laboratory which he had fitted up at home. The records and specimens which he kept show that the number of experimental melts which he made was considerably in excess of 500 and he developed successful formulæ for the production of more than 70 varieties of glasses. Throughout this work he was continually consulted by the glass manufacturers and made frequent visits to glass works to assist in overcoming the inevitable difficulties which arose in the initial stages of production on the large scale. It is impossible to speak too highly of the value and importance of his work on the production of glass during the War period. In recognition of it and of his other war-time services, he was created Knight Commander of the British Empire in 1917 and was elected to Fellowship of the Royal Society during the same year.

In 1919 he delivered the Sir Henry Trueman-Wood Lecture at the Royal Society of Arts, on "Glass and some of its Problems" (1920, 68), and in March, 1927, he gave

a discourse before the Royal Institution on "Some Colouring Agents in Glasses and Glazes."

The reputation which Sir Herbert Jackson had enjoyed for many years among members of the optical industry, enhanced as it was by his war record, led the Council of the British Scientific Instrument Research Association to invite him to become its first Director of Research when the Association was formed in 1918 under the Research Association Scheme of the Department of Scientific and Industrial Research. His analytical habit of mind and his almost intuitive insight into the essentials of a problem, combined with his broad outlook and remarkable experimental ability, fitted him admirably for a position in which the problems to be investigated covered so wide a range. Members of the Association soon came to look upon Sir Herbert Jackson as a friend to whom they could refer almost any problem with the certainty that, although a complete solution might not be immediately forthcoming, he would be able to put forward useful suggestions, or to outline a scheme of investigation which should lead to the problem being rapidly solved. In many cases he would refer to some experiment which he had carried out many years before, would describe the results which he had obtained, and would then suggest that the experiment should be repeated with, perhaps, some modification which would cause it to bear more directly on the problem under consideration. It was difficult at times to realise how one man's experience could have covered so large a range, but his memory was never at fault, and his chemical insight was such that when modifications of his original experiments were tried his predictions were usually found to be correct. In dealing with the widely varied problems put forward by members of the Association, the wealth of information on which Sir Herbert Jackson could draw in this way was invaluable.

Sir Herbert Jackson's interest in clays, porcelains, and glasses led almost inevitably to his taking up the study of ancient glasses and ceramics. His technical knowledge of clays and clay mixtures and of their behaviour at high temperatures, coupled with his skill and experience as a microscopist, enabled him rapidly to discover the nature of bodies and to make a close estimate of the conditions under which they had been fired. Similarly, his knowledge of glasses and of the effects produced by various metallic oxides as colouring agents in glasses of different types, enabled him quickly to identify the nature of a glaze and of the colouring agents used to produce particular effects in glazes. He made a special study of certain Chinese glazes and contributed much valuable information regarding their nature and how they were produced. He also investigated a number of glasses of archæological interest, and, in particular, identified the nature of, and successfully reproduced, a previously unknown scarlet Egyptian glass of ancient origin.

Sir Herbert Jackson had held office as President of the Röntgen Society, 1901—1903, and as President of the Institute of Chemistry from 1918—1921. He was an Honorary Fellow of the Royal Microscopical Society. He was for some time a member of the Senate of the University of London, Governor of the Imperial College, and Chairman of the Technical Optics Committee of the Imperial College. He became a member of the Royal Institution in 1924, and was a Manager of the Institution from 1930—1932 and 1934—1935.

During his period as Director of Research of the British Scientific Instrument Research Association he served on many Government scientific and advisory committees including the Interdepartmental Scientific and Technical Committee on Optical Glass, the Adhesives Committee, the Stone Preservation Committee, the Building Research Advisory Committee, the Advisory Committee on Scientific Research of the London, Midland and Scottish Railway, and others of equal importance.

On his retirement from his position as Director of Research of the British Scientific Instrument Research Association he was appointed Consultant to the Association, and was a member of the Research Committee of the Association up to the time of his death.

He was of a happy disposition, an interesting companion and a man of great personal charm; he will be gratefully remembered by his old students and former colleagues and by a wide circle of other friends.

H. Moore.

## HERBERT EDWARD KIRBY.

### 1859—1937.

HERBERT EDWARD KIRBY, who was born in London on June 22nd, 1859, was educated at the Merchant Taylors' School, and later studied Pharmacy at the School of the Pharmaceutical Society in Bloomsbury Square, passing the Major examination in 1886.

Kirby had been associated for over 60 years with the firm of Messrs. H. and T. Kirby and Co., Ltd., Willesden Green (Manufacturing Chemists), founded by his father; for many years he was the Managing Director, and in 1932 became Chairman on the death of his brother, Sir Woodburn Kirby.

One who knew him intimately writes: "He took little or no part in public affairs but had long been associated with Church and Social work and was particularly interested in the welfare of young people, for whom he always had a kindly word of encouragement and quite a few owe much to his friendship. He was essentially an English gentleman of the old school, a type all too rare in these modern times; his high standard of living was an example and inspiration to everybody who came in contact with him. He was a born optimist and his charm of manner and courtesy made him beloved by all; he will be sadly missed by everyone who knew him." He was in business as usual the day before his death, which took place suddenly from heart failure on August 12th, 1937. He leaves a widow and two adopted sons.

Kirby was elected a Fellow of the Chemical Society on December 2nd, 1886.

H. E. CRESSWELL.

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## DUNCAN SCOTT MACNAIR.

### 1861—1937.

DR. DUNCAN SCOTT MACNAIR, who died at Letchworth on November 27th last at the age of 76, was one of the 12 inspectors appointed in 1893 to take charge of the scientific and technical instruction under the Science and Art Department, which was then being developed.

Macnair was born in Glasgow in 1861, and at an early age showed an enthusiasm for chemistry. He left school at 15 to become assistant in the laboratory of R. Tatlock, the Glasgow City analyst. After three years here, he transferred to the laboratory of the Tharsis Copper Co., and then in 1881 the Government sent him to Cyprus as assistant to the public analyst. A laboratory was established there under great difficulties, but two years later the post was discontinued, and he returned.

For two years he studied chemistry, physics, and mineralogy at Owens College, Manchester, under Sir Henry Roscoe, Professor Schorlemmer, and Sir Arthur Schuster, and he then returned to Glasgow for two years as a teacher in Allan Glen's School, and lecturer in the Glasgow and West of Scotland Technical College.

In 1888 he went to Würzburg and after only one year's study and research under the eminent professor Emil Fischer he was awarded the doctorate "Summa Laude" for work on furfuran and its derivatives.

With these qualifications he took up work in the East London Technical College, now Queen Mary's College, and inspired many students by his teaching. One of his chief discoveries was a method of analysing a mixture of chlorides, bromides, and iodides, at that time a complex problem. During the same year he took the B.Sc. degree with honours at London University when he was specially distinguished in chemistry, being placed second, and qualifying for the University scholarship in that subject.

Three years later, in 1893, he became an inspector, and was appointed to look after the scientific classes in Western, and later in Southern, Scotland. He settled in Edinburgh, and his visits to schools are remembered by many of the teachers for his sympathetic and practical advice. In 1927 he retired and settled at Letchworth, where he had a large circle of friends, who shared in his pleasure in music and games, especially billiards and

golf. He was valued for his generosity, kindliness and helpfulness. He was the author of two school textbooks on science, and for over 50 years a Fellow of the Chemical Society. He married Dora, daughter of Mr. Andrew Matthews, and leaves two sons and a daughter.

A. S. MACNAIR.

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## STEFAN MINOVICI.*

1867—1936.

THE President announced the death at the end of December of Professor Minovici, of the University of Bucharest. M. Delaby, the General Secretary, delivered the following memorial lecture on our eminent Roumanian colleague.

Stefan Minovici was born in 1867 at Râmnicu-Sarat (Roumania). After having successfully passed the examinations for the physicochemical licentiate's degree of the University of Bucharest in 1893, he attended the Chemical Institute in Berlin and for two years filled the position of assistant to the eminent organic chemist, Emil Fischer (1894—1896). His stay in Germany culminated in his obtaining the diploma of Doctor of Chemistry of Berlin University.

On his return to Roumania, Minovici was appointed, almost simultaneously, legal chemist to the Minister of Justice and Professor in the École Supérieure de Pharmacie. Two years later, he became Assistant Professor of the University of Bucharest. In 1911, he was a member of the Higher Council of Industrial Hygiene and in 1912 he became full Professor in the University of Bucharest. Finally the Faculty of Science of the same University entrusted to him the Chair of Organic Chemistry in 1924, and the following year he was appointed Director of the University Chemical Institute.

The work of Stefan Minovici belongs chiefly to the fields of legal chemistry, toxicology and industrial hygiene, of analytical chemistry, which he taught for a number of years, and, lastly, of organic chemistry, in which he was trained at the start of his career during his stay in the laboratory of Emil Fischer.

In the first of these fields he was interested in graphology—he was President of the Roumanian Society of Graphology and a member of the corresponding societies in France and Germany—and he constructed an apparatus for the detection and examination of forgeries in documents; he also studied the application of intense electrical illumination in distinguishing superimposed inks. The problem of the localisation of poisons did not fail to attract his attention: he solved it, for example, in the case of acute poisoning by arsenic and barium; he had also to deal with a case of poisoning by potassium cyanide, and in an instance of mercurial poisoning he studied the action of mercury salts on sheet aluminium. He drew attention to a characteristic and particularly sensitive reaction of picrotoxin; that of an alcoholic solution of anisaldehyde on its sulphuric acid solution. His investigations on the air of Bucharest may also be mentioned in this connexion. Several lectures which Minovici gave can also be cited: blood from the point of view of medico-legal chemistry, legal graphology, alcohol and alcoholism, etc. He was an ardent advocate of the unification of methods of legal arbitration and made a communication on this subject to the Congress of Applied Chemistry held in Rome in 1906.

In analytical chemistry Minovici devoted himself to the determination of certain ions by simple means. Here are some examples: the volumetric determination of potassium by use of the bitartrate, which is titrated acidimetrically, or by precipitation as picrate, with glycerol as the medium; the determination of copper as the ammonia complex $Cu(NH_3)_4SO_4$, which is titrated acidimetrically in presence of methyl-red, and the gravimetric determination of manganese as manganous iodate.

His attraction to organic chemistry is manifest from his first researches. In the year that he took his licentiate's degree (1893), he published his first memoir on the benzenesulphonic esters of the trihalogenated phenols; he nitrated them and showed that, in the esters of trichlorophenol and tribromophenol, nitration took place in the benzene-

* Reprinted by permission from *Bull. Soc. chim.* (Mémoires, 1936, 3, 341) and translated by Dr. H. J. Emeléus.

sulphonic nucleus. He then undertook a series of elegant researches on the aromatic oxazoles and imidazoles, generalising the reaction by which his teacher, Fischer, prepared diphenyloxazole by condensing benzaldehyde with its cyanohydrin, mandelonitrile. In the same way amino-nitriles were found to combine with aldehydes, leading to the corresponding imidazoles, which were also obtained by heating the oxazoles in alcoholic solution with ammonia at 300°. These cyanohydrin condensations were to be studied several times and under varied conditions in the course of his work: in presence of hydrogen chloride a diazine was formed; condensation of aldehydes and cyanohydrins in presence of phosphorus pentachloride gave him compounds formed from two molecules of nitrile and one of the aldehyde; the same condensation in presence of thionyl chloride resulted in other substances produced by the union of two molecules of arylchloroacetamide with one of aldehyde. Minovici was also interested in stereochemical problems and resolved phenylaminoacetic acid, succeeding in obtaining the lævorotatory form; the optical inverse could not be isolated.

These studies and many others which cannot all be mentioned here show that our eminent colleague possessed to a high degree the technique of the organic chemist. But his principal researches were directed towards the study of the constitution, function and metabolism of cholesterol. Numerous derivatives of this sterol, such as halogenated compounds and oxidation products, were obtained in his expert hands, these pioneer researches going back for more than twenty years. Recently Minovici was engaged with the major problem of the origin of cholesterol in the organism, and at the end of last year our sister society, the *Société de Chimie Biologique*, invited him to come and present the main results on this subject before a crowded meeting. The mechanism which he conceived, based on numerous experiments, elucidated the important part played by oleic acid in the formation of cholesterol; in addition, the eminent lecturer developed the relationship between squalene and cholesterol. In presenting the Pasteur Medal to him as a token of appreciation and admiration, the President, M. Baudouin, invited him to return to France, where he loved to stay, and give an account of the conclusion of these researches. An implacable destiny determined otherwise, however. He had also commenced some studies on the bile acids, the relationship of which to the sterols has now been demonstrated.

We cannot recall here all the researches emanating from the hive which the laboratory of analytical chemistry and the laboratory of organic chemistry of the Faculty of Sciences of Bucharest became under the energetic leadership of Stefan Minovici. A hundred original memoirs with the most diverse themes are listed in a review, which appeared last year, of the scientific activity of the master who presided with such distinction over the destinies of Chemistry in this friendly nation.

What may be said, too, of his teaching work? Four important volumes have come from his authoritative pen, forming a treatise on analysis which the author modestly entitles "Theoretical and Practical Manual of Analytical Chemistry": one volume is devoted to qualitative analysis, a second to quantitative analysis (gravimetric, volumetric, electrometric and gasometric), a third to toxicology, and the last to biological analysis.

Many scientific societies have been honoured in counting him among their members. In the Roumanian Chemical Society Minovici played a very prominent part: he was its general secretary, and was its president when the sad news of his death came to us. A member of our Society since 1912, he reserved from time to time for our *Bulletin* the first communication of his publications. The Council has shown its sympathy and admiration for our colleague by making him an Honorary Member of our Society and by offering him the medal struck with the effigy of Lavoisier. The Biological Society of London and the Polish Chemical Society also bestowed on him the title of Honorary Member.

The Roumanian Government appointed him as a delegate at numerous international gatherings: at the International Congress of Applied Chemistry held in Vienna (1898), in Paris (1900), in Berlin (1903), and in Rome (1906); then, after the war, at the Congress of the International Union of Chemistry at Brussels (1921), Lyon (1922), Cambridge (1923), Copenhagen (1924), Washington (1926), Madrid (1934), etc. . . . In 1925 he was nominated vice-president of this organisation.

He often came to France, and took a very active part in various chemical gatherings:

as a token of recognition of his loyalty to our country, the French Government appointed Stefan Minovici an Officer of the Legion of Honour.

We reiterate to the Roumanian Chemical Society, to the University of Bucharest, and to the family of our eminent colleague the very sincere condolences of the French Chemical Society. They have been presented verbally at the funeral of Professor Minovici by our colleague M. Fabre, General Secretary of the Société de Chimie Biologique, who was in Roumania at the time, and was kind enough to represent us.

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## ARTHUR WILLIAMS MORGAN.

1892—1937.

In the death of Arthur Williams Morgan on October 10th, 1937, at the early age of 45, the world of science in general and of pharmacy in particular, lost one of its most gifted and charming men. His was a type of personality encountered only too infrequently. Always bright and cheerful, ready with advice and help whenever they were needed, one always felt the better for "a word with Morgan."

Born in South Wales, Morgan was attracted to pharmacy and in due course became a Member of the Pharmaceutical Society. During the Great War he served in the Royal Army Medical Corps from 1914 to 1916, being then invalided out. After the War he settled in Bedford and in addition to guiding the destinies of three pharmacies, found time for many public activities. He was President of the Local Branch of the Pharmaceutical Society, a Governor of the Harpur Trust and a member of the Advisory Committee of Bedford Technical School. Until forced to resign owing to ill health, he was a member of the Rotary Club of Bedford.

The funeral service took place at Holy Trinity Church, Bedford, and was attended by representatives of the various public bodies, of the town and county, in which Mr. Morgan was interested. He was elected a Fellow of the Chemical Society in December, 1929.

F. H. Webb.

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## FREDERICK CHARLES THOMPSON.

*1891—1937.*

Frederick Charles Thompson, M.Sc., died on September 4th, 1937, at the age of forty-six years. Born in Lancashire, he moved to Leeds at an early age and spent the greater part of his life in this city. He attended the Cockburn High School and in 1908 was awarded a City of Leeds Scholarship tenable at Leeds University. Two years after graduating with an honours degree in chemistry, he obtained an honours degree in the Chemistry of Leather Manufacture, and later was admitted to the degree of Master of Science of Leeds University. In 1913 he was appointed demonstrator in the Leather Industries department under the late Professor H. R. Procter, D.Sc., F.R.S. He became lecturer in 1925 and in the meantime had been appointed to the position of research assistant in the Procter International Research Laboratory. Keenly interested in the applications of protein chemistry, he carried out a number of investigations independently and in collaboration with Professors H. R. Procter and D. McCandlish, and Mr. W. R. Atkin. He was associated with the publication of more than thirty papers, the majority of which appeared in the *Journal* of the International Society of Leather Trades' Chemists. A complete list of his publications is to be found in the October (1937) issue of that journal. Thompson was actively interested in the Leather Chemists' Society, and after serving as chairman of several of its commissions, was elected to the Presidency in 1932. Much of his work was of scientific and practical importance. For example, it had long been known that methods of assessing the acidity of vegetable-tanned leather left much to be desired. Working in conjunction with his colleague W. R. Atkin, a method was devised for determining in a reliable manner the "acid value" of leather. It was shown that strong acids could only be present in harmful quantities when

the $p_H$ of the leather was lower than a suggested value, as determined by the Atkin–Thompson method. Shortly after this method was published it was incorporated in British government specifications, as it offers a reliable means of assessing the liability of vegetable-tanned leather to undergo acid deterioration—a matter of particular importance in leathers used by the fighting services.

In the quantitative determination of tannin in commercial tanning materials, a disintegrated purified raw hide powder is used as a reagent in the official method of analysis. Considerable difficulty and many disputes arose through some unknown variable in successive lots of the material prepared by the authorised manufacturers, which caused the official method of analysis to show disturbing differences in tannin content in a given sample of tanning material. An ingenious investigation by Thompson and Atkin established the trouble as being due to a small variation in the calcium content of different hide powders. As a direct result of this work, a uniform supply of hide powder has become available to leather chemists throughout the world, and a much greater degree of concordance has been secured in the assessment of commercial tanning materials than was previously possible.

In recent years Thompson collaborated with Dr. J. Gordon of the Leeds University Medical School in research upon the complex subject of immunity, and several of their papers have been published in the *British Journal of Experimental Pathology*.

Thompson had many University activities as tutor and member of the local Committee of the Association of University Teachers. His other interests were varied but chiefly connected with the Boys' Brigade and music. As a violinist he was associated with several local amateur orchestras. He married in 1919, and his wife survives him.

D. McCANDLISH.

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## GEORGE RICHARD TWEEDIE.

1857—1937.

GEORGE RICHARD TWEEDIE, of "Meadlands," Hillborough, who died at his residence on October 17th, 1937, aged 80, was a Justice of the Peace for the Liberties of the Cinque Ports and had been a Fellow of the Chemical Society since June, 1879. Born in London, his father was William Tweedie, a Scotsman, at one time Publisher in the Strand and the originator of the A.B.C. Time-Table, besides an ardent Temperance Reformer. Trained as an analytical chemist at the Regent Street Polytechnic, Tweedie was for many years a lecturer on popular chemistry, witchcraft and folklore, besides practising and teaching chemistry in the Isle of Thanet, where he resided between 1886 and 1899. He was a keen member and one time President of the local photographic Society of that period when the art was in its infancy.

Keenly interested in politics, and the Liberal Party of those days, he took up political work in 1892 and was associated as agent with Parliamentary elections in that period in Thanet, Isle of Wight, Romford, etc.

He married first in 1883, Alice Mary, daughter of Alderman John Dunning of Middlesborough, Yorks, by whom he had a son and a daughter who both survive him. John Dunning was an ironmaster, a Militant Quaker and associated with the Peases. Not being a Member of the Society of Friends, a good deal of procedure was necessary to enable Tweedie to marry a Quakeress. Moving to South Bucks in 1900, living at High Wycombe, Marlow and Slough, as Liberal Agent he fought elections on behalf of Sir John Thomas and Arnold Herbert which brought him into contact with many well-known men of the day. Leaving South Bucks in 1910, he resided in the New Forest for some years and then moved to Southfields, London, and during the War was able to do useful work as a chemist on the staff of a large manufacturer.

His first wife died in 1919, and in 1921 he married Miss Emily H. Douse at Wimbledon Park. In 1924 he moved to Hillborough, Herne Bay, where he resided until his death.

He was the author of many articles on diverse subjects and his two books "Hampshire's Glorious Wilderness" and "Yesterday" show him a master of English and the possessor

of an acute mind and retentive memory. A man of high principle, teetotaller and non-smoker, kindly, with a strong sense of humour, he was greatly esteemed. Deafness during his later years prevented active participation in public affairs.

M. G. TWEEDIE.

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## JOHN AUGUSTUS VOELCKER.

1854—1937.

DR. J. A. VOELCKER, who died on November 6th, in his eighty-fourth year, was the second of the five sons of the late Dr. Augustus Voelcker, F.R.S. He was born on June 24th, 1854, at Cirencester, where his father was Professor of Chemistry in the Royal Agricultural College, and some of his early schooldays were spent at a preparatory school in the not distant town of Berkeley. In 1864 his father—who had become Consulting Chemist to the Royal Agricultural Society in succession to the late Professor Way—resigned his professorship and removed to London, where the education of his sons was continued at University College School. At the end of his school course, where he began chemistry under the late Temple Orme, John went on to University College, where he took successively (with Honours) the degrees of B.A. aud B.Sc., his chemical teacher being the late Professor Williamson. During his studentship most of his vacations and other available "off-times" were spent in the laboratory of his father in Salisbury Square, Fleet Street, and as it happened that the writer of this notice was at that time a pupil of Dr. Augustus Voelcker this led to an early and lifelong friendship.

During Voelcker's years at University College he found an outlet for physical energy on the racing track, establishing a reputation as a long-distance runner and becoming the first secretary of the College and Hospital Sports Club. His interest in athletics was maintained throughout his life, he having been an active member of the Committee of the London Athletic Club (of which he was twice President) and of the Thames Hare and Hounds, whose cross-country runs he rarely failed to attend. When the natural waning of muscular adaptability reduced his personal participation in the more strenuous forms of athletics to that of an interested spectator he took up shooting and fishing as his outdoor recreations and became skilled with the "dry fly." This reference to the sporting side of his life is made here because the writer considers that it was not without its bearing on his character and life-work.

On leaving University College Voelcker went to Giessen, where he took chemistry under Professor Naumann and agriculture under Professor Thaer, and obtained his doctor's degree for a dissertation dealing with the molecular composition of apatite and other forms of naturally occurring calcium phosphate. Later in life, on the occasion of the visit of the Royal Agricultural Society to Cambridge in 1894, he received from that University the Honorary Degree of M.A.

After his career at Giessen he returned to work with his father, by whom he and his brother E. W. Voelcker were later taken into partnership under the title of Dr. Augustus Voelcker & Sons.

Some time before this the laboratory in Salisbury Square had become supplemented by a second laboratory built as an annexe at the rear of the premises of the Royal Agricultural Society in Hanover Square, and it was chiefly here that Voelcker worked until the death of his father in December, 1884, when he was appointed in succession to him as Consulting Chemist to the Society, an appointment which he held up to the time of his death, covering a period of over fifty years.

During this long tenure of office he naturally came into personal association with most of the well-known leaders of agricultural thought and practice and had opportunities of visiting farms in most parts of the country and of familiarising himself with diverse systems of husbandry and stock management. Of these opportunities he was keen to avail himself, and he had a characteristic habit of making meticulous notes of all that he observed, preserving them for reference in his advisory work which brought him a constant flow

of correspondence; and the advice that he was able to give soon came to be generally received with well-justified confidence.

In addition to the busy routine of analytical and advisory work for members of the Royal Agricultural Society there devolved upon him, immediately on his appointment, the no light burden of the virtual direction and management of the Woburn Experimental Station at Crawley Mill Farm, which had been established in 1876 on the estate of the Duke of Bedford and carried on up to this time under the superintendence of his father in association with the Council's Chemical Committee.

The expenses of this station were defrayed by the Duke of Bedford up to the year 1910, when his financial support was discontinued in view of a grant of £500 per annum made by the then newly established Development Commission. All further expenditure on the farm and station was undertaken by the Society up to the year 1921, when its Council unfortunately decided to abandon the work. Hereupon Voelcker, loath to contemplate the "scrapping" of Woburn and all that it stood for, courageously obtained from the Duke of Bedford the transference of the lease of the farm to himself, and with monetarily self-sacrificing devotion and with only the aid of the grant of the Development Commission carried it on at his own risk for five years until, in 1926, it was taken over by the Lawes Agricultural Trust. Voelcker, however, remained Honorary Director of the Station until 1936.

The establishment of the Woburn Station was originally for the purpose of practically testing the comparative residual manurial value of highly nitrogenous and low nitrogenous feeding stuffs from the point of view of compensation to outgoing tenants for foods consumed on the farm, in view of the conclusions derived from the earlier work of Lawes and Gilbert; and, incidentally, for the repetition, on a very different type of soil, of the experiments on the continuous growth of grain crops which had long been carried out by Lawes and Gilbert at Rothamsted; but much other experimental field work had been added from time to time. A further important addition to the Woburn investigations was made in 1897 by the bequest to the Royal Agricultural Society of £10,000 by the late Mr. E. H. Hills, for the purpose of experiments on the influence on plants and soils of what were then regarded as less commonly occurring chemical elements. This led to the establishment of a local laboratory and pot-culture station. Investigations under this bequest were carried on by Voelcker for twenty-three years with the local assistance at first of Dr. H. H. Mann, and later, successively, of H. M. Freear, J. Crabtree and A. Blenkinsop, until, in 1921 the Society, on relinquishing its connection with Woburn, made over the Hills Bequest to the University of Cambridge. Up to this time the multifarious Woburn researches, both in the field and in the pot-culture station, were recorded yearly in the long series of reports by Voelcker printed in the volumes of the *Journal* of the Royal Agricultural Society, and were, perhaps, not very much known outside of the circle of readers of that Journal. The side of the work constituting the field experiments has, however, been lately focused (in 1936) in the volume of "Fifty Years of Field Experiments at the Woburn Experimental Station" by Sir John Russell and Dr. Voelcker.

As regards the primary original object of the field experiments the results have been of momentous, and at the same time disappointing, interest inasmuch as that they have persistently indicated that, at any rate, on the type of land exemplified by the light Woburn soil, the superiority of the residual manurial effect of feeding-stuffs rich in nitrogen as compared with those of the less nitrogenous and more farinaceous foods has not been in accord with long established assumption. Apart from the Woburn results investigation at Rothamsted and elsewhere on the composition of farmyard manure as affected by the foodstuffs consumed in making it and by the chemical changes incidental to its storage, had been leading to the conclusion that the original tables of Lawes and Gilbert, bearing upon the question of compensation to outgoing tenants for the unexhausted value of their contributions to the soil, called for revision. This revision was undertaken by Voelcker and Sir A. D. Hall, whose modified compensation tables were published in a joint paper in the *Journal* of the R.A.S.E. for 1902. A further paper on the subject by Voelcker and Hall appeared later in the *Journal* of the R.A.S.E. for 1913, in which still further modifications were made of the earlier tables, and this later version, with revision from time to time

by Voelcker in view of fluctuations in the market value of nitrogenous, phosphatic and potassic fertilisers, is still generally accepted in England for compensation valuations by the Central Association of Tenant-Right Valuers; but the practical experience on the Woburn Farm has done much to emphasise the danger of their too literal application without regard to variations of soil and local conditions.

One of the most spectacular results in Voelcker's field work on the Woburn Farm was the demonstration that the long-continued use of sulphate of ammonia on soil deficient in lime may result in the almost complete suspension of fertility owing to the leaching out of the original lime of the soil in the form of soluble calcium sulphate; with, however, the further consolatory experience that fertility could be completely and promptly restored by a dressing of lime, thus indicating the simple means by which the otherwise beneficent effects of sulphate of ammonia can be enjoyed on land naturally poor in lime without fear of deterioration.

The recent book of Russell and Voelcker contains no record—beyond a mere passing reference—of the special pot-culture work carried out under the Hills Bequest; but a brief summarised account of it was contributed by Voelcker himself to the R.A.S.E. *Journal* for 1923. The special elements or substances of which the effects were tested included manganese, lithium, barium, cæsium, cerium, strontium, lead, zinc, tin, chromium, copper, boron, arsenic, iodine, bromine, fluorine, and " radio-active " ores.

An important temporary diversion of Voelcker's activity occurred in 1889, when, at the request of the Indian Government, the Secretary of State for India decided to send out from England an agricultural chemist to make a tour of enquiry in India and to advise upon the course to be pursued for possible improvements in Indian agriculture. For this duty, on the recommendation of the late Sir James Caird, Voelcker was chosen and, with the permission of the Society, he visited India and spent a full year making two extensive tours of the Empire. The result was a report of some 450 pages on " The Improvement of Indian Agriculture " (Eyre & Spottiswoode, 1894). This report had a far-reaching effect on the subsequent development of Indian agricultural education and of the pursuit there of agricultural chemistry, largely encouraged by the work carried on for many years in India by Voelcker's former assistant, the late Dr. Leather, who was sent out as an immediate consequence of Voelcker's report. Although Voelcker's report was received at the time with much congratulatory approbation, the conferment on its author of the distinction of C.I.E. was delayed until as recently as 1928; it was then given presumably as a consequence of a new enquiry instituted under the auspices of Lord Linlithgow, when attention was redirected to the report of 1894.

Voelcker had been a member of the Chemical Society for fifty-three years and served on its Council in 1891 to 1895 and 1902 to 1904. In earlier days he was a constant attendant at our meetings and usually contributed to the discussions on any matters relating to agricultural chemistry, but he made no contribution to our *Journal* for the reason that the main results of his research work were, as has been already mentioned, contributed to the *Journal* of the Royal Agricultural Society. He was one of the leading members of the Society of Public Analysts, and occupied its presidential chair in 1901 to 1902. For many years and up to the time of his death he was a member of the Committee of the London Farmers' Club, of which, in 1908, he was elected Chairman, a distinction which he especially valued in view of his father having occupied the same position thirty-three years earlier. He was also a member of the Advisory Committee appointed to assist the Ministry of Agriculture under the Fertilisers and Feeding Stuffs Act of 1926.

He was consulting chemist to the Royal Horticultural Society, as well as to the Royal Agricultural Society, and also to the Bath and West of England Society; and he acted as Official Agricultural Analyst for Buckinghamshire, Oxfordshire, Middlesex, Northamptonshire, Northumberland, the East Riding of Yorks, the Isle of Ely, and the County Borough of Oxford. Under the Food and Drugs (Adulteration) Act he was (jointly with his nephew, Mr. Eric Voelcker) Public Analyst for the Counties of Northampton, Buckingham and Oxford, and for the County Borough of Banbury.

This notice would be incomplete without reference to yet another side of his activity which the writer feels that he would not have liked to be left unrecorded. When his father

came over from Germany he settled first in Edinburgh and there became a devoted adherent of the Presbyterian Church. His religious enthusiasm was passed on to his son, who was an active member of the congregation of St. John's Presbyterian Church, Kensington, which he attended regularly from 1870 onwards. He became a deacon in 1884, and an elder in 1897, acting for the last twenty-four years as Sessions Clerk; and he did much outside work in connection with church extension in the community to which he belonged. Strong, however, as was his own religious conviction, this was unmarred by sectarian prejudice or by lack of tolerance for views which differed in religious or philosophical complexion from his own.

In personal and professional matters his attitude was always dominated by a strict sense of truth and straightforwardness, and there were sometimes occasions when, in matters of scientific interpretation or of administrative policy, he found it not easy to yield to argument based on views which happened not to be consonant with those to which he had felt himself conscientiously impelled. But any differences which thus arose were seldom allowed to interfere with personal friendship, and his essential amiability of character was aided by the possession of a happy endowment of that sense which sometimes throws oil on troubled waters—the sense of humour. The knowledge acquired during his long and wide experience was always ungrudgingly placed at the disposal of any colleague who sought his advice or assistance; and his genial presence and handsome figure—bowed a little in his declining years—as well as his loyal friendship will be affectionately remembered by very many and—if he may be forgiven for yet another personal allusion—by none more than the writer.

Voelcker married in 1884 Alice, eldest daughter of the late Mr. W. Westgarth, formerly of Melbourne, and leaves one son and two daughters. His eldest son died in early infancy, and his second son lost his life in the War.

BERNARD DYER.

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## JEAN BAPTISTE SENDERENS.

1856—1937.

JEAN BAPTISTE SENDERENS was born in 1856 at Barbachen, a small village in the canton of Rabastens-de-Bigorre in the Hautes-Pyrénées. He was educated at the Collège de Garaison and at the Institut Catholique at Toulouse, where he obtained his licentiate and doctorate in science and subsequently the licentiate and doctorate in philosophy. While still a student, Senderens attracted the attention of E. Filhol, then professor in the faculty of science at Toulouse; and much of his earlier work was the result of this collaboration. Senderens remained at Toulouse, as professor of chemistry, until the war, when he became attached to the Poulenc factory at Vitry-sur-Seine. Finally, with advancing years, he returned to Barbachen, not however to rest but rather to continue working, in the well-equipped laboratory which he had set up, in the peace of his native village, where he died on September 26th, 1937, at the age of 81. Senderens was in holy orders, and became first an abbé and later a canon. He was the recipient of many honours. He shared with Sabatier the Jecker prize in 1905; and he was a chevalier of the Légion d'Honneur and membre correspondant of the Académie des Sciences; but his lasting memorial, linked with that of Sabatier, will for all time be found in the wide and ever increasing application of catalytic hydrogenation—above all with nickel—both in general chemistry and in industry. He was elected an honorary Fellow of the Chemical Society on March 18th, 1920.

Senderens' scientific work may be divided into three periods, corresponding to his association with Filhol, with Sabatier, and to a later period during which he worked both independently and together with Aboulenc, largely on catalytic dehydration and esterification. His first paper, published with Filhol in the *Comptes rendus* in 1882, contained a study of the action of sulphur on solutions of metallic salts; and this was followed by a series dealing with similar reactions and with various phosphates, arsenates

and antimony compounds. So far, although his papers show signs of clear thought and careful experimental technique, his career had been relatively uneventful.

His collaboration with Paul Sabatier, which was to give rise to the work with which his name is chiefly associated, began in 1892 with an investigation of the action of oxides of nitrogen on metals, in the course of which it was observed that reduced copper or cobalt absorbs nitrogen peroxide with the formation of so-called nitro-copper or nitro-cobalt. This work may be regarded as the direct precursor of that on catalytic hydrogenation; for, on substituting ethylene for oxides of nitrogen and leading this gas over finely divided nickel with the object of seeing whether addition products similar to those formed by copper with nitrogen peroxide or by nickel with carbon monoxide could be obtained, it was fonnd that decomposition of ethylene occurred, accompanied by the formation of ethane and other products. The possibility of the hydrogenation of ethylene was realised; and, in the same year, Sabatier and Senderens showed experimentally that ethane could be prepared smoothly and quantitatively by leading a mixture of ethylene with an excess of hydrogen over nickel which had been freshly reduced from its oxide at a moderate temperature. Further work showed that cobalt, copper and iron, in addition to platinum, possessed the same properties as nickel, and that the reaction was a general one which could be applied not only to ethylene but also to its homologues and to other unsaturated compounds, including acetylene and its derivatives. It may be noted that, while Sabatier and Senderens were undoubtedly the discoverers of the hydrogen-activating properties of the nickel group of hydrogenation catalysts, the catalytic activity of platinum for the hydrogenation of acetylene to ethane had been noticed by de Wilde in 1874.

An extension which had the widest influence in organic chemistry generally began with the employment, in 1901, of nickel for the hydrogenation of benzene. It was found that *cyclo*hexane, which had previously been made with difficulty by the reduction of benzene with hydriodic acid, could be easily prepared by leading a mixture of benzene and hydrogen over nickel. Cobalt and platinum-black were, under Sabatier and Senderens' conditions, less satisfactory catalysts, and iron, copper and platinum sponge were stated to be relatively inactive; but the reaction was, as before, found to be a general one which could be used for the hydrogenation of benzene homologues as well as for condensed rings such as naphthalene: further, it was observed that the hydrogenation of an aromatic ring was readily reversible and that it differs in this respect from the hydrogenation of an ethylenic or acetylenic bond in an aliphatic chain.

The next step was the catalytic reduction of oxygen-containing groups. Nitrobenzene was, as was to be expected, easily reduced catalytically; but, under Sabatier and Senderens' conditions of working, there was a tendency towards the reduction also of the ring, with formation of *cyclo*hexylamine and condensation products. More important from a preparative standpoint, since it could not be obtained by reduction with nascent hydrogen, was the production of methane by the hydrogenation of carbon monoxide or dioxide with nickel or cobalt. Copper, on the other hand, was found only to cause the reduction of carbon dioxide to monoxide; and the somewhat milder hydrogenating properties of this metal, compared with nickel, were also utilised in other reactions in which stepwise hydrogenation is possible. Thus, styrene was converted principally into ethylbenzene on hydrogenation with copper, whereas nickel induced the saturation also of the ring, with production of ethyl*cyclo*hexane; and amylacetylene gave, respectively, amylethylene and the saturated paraffin.

In 1903, Sabatier and Senderens investigated the hydrogenation of phenol. In the presence of nickel, this was converted into *cyclo*hexanol, which, at higher temperatures, passed by loss of hydrogen into *cyclo*hexanone; but, by selecting the conditions and the catalyst, either substance could be obtained. In the same year the catalytic reduction of aldehydes and ketones was studied. Benzaldehyde, on being hydrogenated with nickel, gave principally toluene, the oxygen being removed, and there was some decomposition to benzene; but acetone and other aliphatic ketones, which were hydrogenated by Sabatier and Senderens at a somewhat lower temperature, readily gave *iso*propyl alcohol and its homologues, the oxygen being retained; and later work showed that the production

of hydrocarbon or of an alcohol was a function of the activity of the catalyst and of the temperature. Work was also carried out on the reversed reaction, namely, on the dehydrogenation of alcohols to aldehydes or ketones by passage over finely divided metals.

Sabatier and Senderens had by this time built up a far-reaching structure, which was only limited by their adherence to their original hydrogenation technique. This involved in each case the passage of the substance to be hydrogenated, as a vapour or gas, over the catalytic metal; and, consequently, the enlargement of scope brought about by liquid-phase hydrogenation was left to others. A direct industrial extension of Sabatier and Senderens' work was made in about 1910 (although the first relevant patent dates from 1903) by the employment of nickel for the large-scale hydrogenation of unsaturated glycerides for the production of so-called hardened oils, a process which has become of primary importance in the oil industry both as a manufacturing method and as a control of the price of natural stearin.

In about 1907, Senderens turned from the further development of hydrogenation to the study of catalytic dehydration. The dehydration of alcohols to ethylenic hydrocarbons or, at lower temperatures, to ethers, by passage over catalysts such as alumina, aluminium sulphate, aluminium silicate and silica, was examined; and the results obtained did much to extend and systematise our knowledge of a field which had already been investigated to some extent by, for instance, Ipatiev. A further reaction to be examined in considerable detail by Senderens was the production of ketones by the elimination of carbon dioxide from carboxylic acids. Squibb had shown, in 1895, that acetone was formed by leading the vapour of acetic acid over heated calcium oxide or carbonate. Senderens studied first the use of alumina and, later, that of thoria or zirconia. Of these substances, thoria was found to be most effective, and the reaction was extended to the general preparation of higher and of mixed ketones, also of aldehydes. At about this time (1911) Senderens' collaboration with Aboulenc began with the publication of a series of papers on catalytic esterification.

Then came the war. Save for a single paper in 1915 on the employment of nickel and of nickel oxide as catalysts, Senderens' time became occupied by his work at Vitry; and for approximately five years no further papers appeared. During his stay at the Poulenc works, his personality won for him the friendship of many among the staff and directors, especially that of M. Camille Poulenc.

Much of Senderens' work in the years immediately following the war consisted of further studies of catalytic dehydration, carried out in many cases in collaboration with Aboulenc; but he also continued, to some extent, the development of hydrogenation, and an interesting departure from his vapour-phase technique is given by his work on the catalytic hydrogenation of lactose and of polyphenols, which was carried out in the liquid phase. Senderens continued each year to contribute papers, principally on catalytic subjects, his final work being on the elimination of hydrogen halides from monohalogenoparaffins such as propyl chloride, and on some reactions of benzoyl chloride (*Compt. rend.*, 1937, **204**, 1296), published when he was over 80. He thus was able to work effectively up to the time of his death, and he died in full possession of the clearness of thought and the high degree of manipulative skill which had always distinguished him.

By his death we have lost the co-founder of a completely new section of chemical knowledge. Whether or not this knowledge of catalytic hydrogenation would have come in the course of natural evolution, had not Sabatier and Senderens chanced to investigate the action of ethylene on nickel, it is difficult to say; but, certainly, by virtue of the pioneering work of these two investigators immediately before and during the early years of the century, the foundations of catalytic hydrogenation were securely laid. The world is poorer for the passing of a great experimentalist.

E. B. MAXTED.

# 28. *Nitration of* m-*Methoxycinnamic Acid.*

By S. N. Chakravarti, K. Ganapati, and S. Aravamudhachari.

Contrary to the predictions of the current theories, *4-nitro-3-methoxycinnamic acid*, m. p. 296°, is the main product of nitration of *m*-methoxycinnamic acid. Its constitution has been established by its oxidation to 4-nitro-3-methoxybenzaldehyde and 4-nitro-3-methoxybenzoic acid, and by synthesis. *6-Nitro-3-methoxycinnamic acid*, m.p. 227°, and *2-nitro-3-methoxycinnamic acid*, m. p. 265°, also formed during the nitration, have been synthesised.

As bromination of *m*-methoxycinnamic acid (Davies and Davies, J., 1928, 602; see also Jones and James, J., 1935, 1602) gives exclusively 6-bromo-3-methoxycinnamic acid, it was hoped that 6-nitro-3-methoxycinnamic acid, required for synthetical work on alkaloids, might be obtained in good yield by its nitration. The main product, however, formed under a variety of conditions was, contrary to the predictions of the current theories, *4-nitro-3-methoxycinnamic acid*, m. p. 296°, giving on oxidation 4-nitro-3-methoxybenzaldehyde and 4-nitro-3-methoxybenzoic acid. 6-*Nitro*- and 2-*nitro-3-methoxycinnamic acids* were formed only in small quantities. The constitutions of the three nitro-compounds were established by synthesis.

Much of the older work (see Reiche, *Ber.*, 1889, **22**, 2358) on the nitration of *m*-hydroxycinnamic acid and *m*-methoxycinnamic ester requires revision and correction: this will form the subject of a future communication.

## Experimental.

*m*-Methoxycinnamic acid was nitrated with an excess of nitric acid (*d* 1·42, 1·48, or 1·52), alone or in presence of glacial acetic acid or sulphuric acid. Fuming nitric acid produced dinitration. Mononitration was best carried out as follows: *m*-Methoxycinnamic acid (10 g.) was gradually added to nitric acid (50 c.c., *d* 1·48) at 0° and after 15 minutes' stirring the mixture was poured into cold water. The precipitated acids were washed with water and fractionally crystallised from acetic acid. The first acid to separate (yield, 70—80%) had m. p. 296° (shrinking at 280°) (Found: C, 53·8; H, 4·2; N, 6·5. $C_{10}H_9O_5N$ requires C, 53·8; H, 4·0; N, 6·3%) and formed a methyl ester, m. p. 163°. From the mother-liquor, an acid, m. p. 265°, and an acid, m. p. 227°, were ultimately isolated (methyl esters, m. p. 116° and 128° respectively): separation of the acids in the form of their methyl esters also necessitated tedious fractional crystallisations.

*Identification of the Acid, m. p.* 296°.—(a) The acid (1 g.) was dissolved in sodium carbonate solution and treated with potassium permanganate (1·2 g. in 20 c.c. of water), and the whole boiled until the colour of the permanganate vanished. On acidification of the cooled filtered solution, 4-nitro-3-methoxybenzoic acid was precipitated; it crystallised from water in long needles, m. p. 233° alone or mixed with an authentic specimen prepared from 4-nitro-3-methoxybenzaldehyde.

(b) The acid (0·5 g.), dissolved in dilute sodium carbonate solution, was gradually treated with a 2% solution of potassium permanganate (45 c.c.) in presence of benzene, in which the resulting aldehyde dissolved as soon as it was formed. When the permanganate was decolorised, the liquids were filtered, the precipitate washed several times with benzene, and the combined benzene solutions dried over sodium sulphate and evaporated. The residue crystallised in needles of 4-nitro-3-methoxybenzaldehyde, m. p. and mixed m. p. 104° (oxime, m. p. 147°).

The above proofs that the acid, m. p. 296°, is *4-nitro-3-methoxycinnamic acid* were confirmed by the synthesis of the acid.

The 6-nitro-compound was obtained in better yields by the nitration of *m*-methoxycinnamic ester than by the nitration of the acid itself.

*Synthesis of the Nitro-*m*-methoxycinnamic Acids.*—*m*-Hydroxybenzaldehyde was nitrated (Pschorr, *Ber.*, 1901, **34**, 4400) and 4-nitro- and 6-nitro-3-hydroxybenzaldehyde were isolated (Friedländer and Schenck, *Ber.*, 1914, **47**, 3046), and methylated, the former with methyl sulphate and sodium bicarbonate solution, and the latter with methyl sulphate and sodium hydroxide solution. 2-Nitro-3-methoxybenzaldehyde was prepared by nitrating *m*-methoxybenzaldehyde under conditions similar to those used by Hinkel, Ayling, and Morgan (J., 1932, 1115).

The above three nitro-*m*-methoxybenzaldehydes were converted into the corresponding

cinnamic acids in almost quantitative yields by the following method : The aldehyde (13 g.), malonic acid (16 g.), pyridine (25 c.c.), and piperidine (1 c.c.) were heated on the steam-bath for 1½ hours and then boiled for 10 minutes. When the product was poured into dilute hydrochloric acid, the cinnamic acid was precipitated. It was crystallised from acetic acid.

*4-Nitro-3-methoxycinnamic acid*, m. p. 296° (shrinking at 280°) (Found : N, 6·5. Calc. : N, 6·3%), was converted into its *methyl* ester, m. p. 163° (Found : N, 6·1. $C_{11}H_{11}O_5N$ requires N, 5·9%). *2-Nitro-3-methoxycinnamic acid*, m. p. 265° (Found : C, 53·9; H, 4·3. $C_{10}H_9O_5N$ requires C, 53·8; H, 4·0%), gave a *methyl* ester, m.p. 116° (Found : N, 6·0%). *6-Nitro-3-methoxycinnamic acid*, m. p. 227° (Found : C, 53·7; H, 4·2%), formed a methyl ester, m. p. 128°. In all three cases the m. p.'s of the acid and its ester were not depressed by the corresponding nitration acid and its methyl ester respectively.

*4-Nitro-3-hydroxycinnamic acid*, m. p. 248° (Found : N, 6·9. $C_9H_7O_5N$ requires N, 6·7%), and *6-nitro-3-hydroxycinnamic acid*, m. p. 221° (Found : N, 6·8%), also were synthesised by the malonic acid–pyridine method.

Annamalai University, Annamalainagar,
Chemical Examiner's Laboratory, Agra. [*Received, August 4th,* 1937.]

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## 29. *Synthetical Experiments in the Paraberine Group. Part II. Synthesis of* 17-*Keto*-3 : 12-*dimethoxy*-6 : 15 : 16 : 17-*tetrahydroparaberine*.

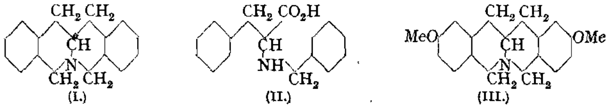
By S. N. Chakravarti and P. L. N. Rao.

To throw light on the preferential selection of angular structures by Nature, attempts were made to synthesise compounds of the type of paraberine having linear structures. The synthesis of tetrahydroparaberine (i) from dibenzylmethylamine by the action of formaldehyde or through its formyl derivative and (ii) from dl-β-*phenyl-N-benzylalanine* could not be achieved. Attempts were next made to prepare suitable dimethoxytetrahydroparaberines, which might be more amenable to synthesis owing to the presence of activating *p*-methoxy-groups.

β-3-*Methoxyphenylalanine* was synthesised, and its formyl derivative converted into N-*formyl*-β-3-*methoxyphenyl*-N-3′-*methoxybenzylalanine* by the action of 3-methoxybenzyl chloride. The formyl compound after hydrolysis was converted into 6-methoxy-2-3′-methoxybenzyl-1 : 2 : 3 : 4-tetrahydro*iso*quinoline-3-carboxylic acid by the action of formaldehyde. This acid, which was also synthesised by another method, on cyclisation with 70% sulphuric acid gave 17-keto-3 : 12-dimethoxy-6 : 15 : 16 : 17-tetrahydroparaberine in about 15% yield.

In Part I (*J. Annamalai Univ.*, 1934, **3**, 208), the synthesis of 8 : 17-diketo-6 : 17-dihydroparaberine was described. During the final ring closure, an unexpectedly high yield of about 60% was obtained, which was not quite in conformity with the ideas expressed by Campbell, Haworth, and Perkin (J., 1926, 32) and was probably due to stereochemical differences introduced by the presence of a double bond. To throw further light on the problem of ease of formation of compounds having linear structures, the synthesis of tetrahydroparaberine (I) and its 2 : 12-(III) and 3 : 12-dimethoxy-derivatives was attempted.

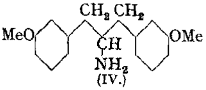
The synthesis of (I) from dl-β-*phenyl*-N-*benzylalanine* (II) could not be achieved. The synthesis of 2 : 12-dimethoxytetrahydroparaberine (III) was next attempted because it might be facilitated by the presence of the activating *p*-methoxy-groups. The requisite



(I.) (II.) (III.)

αγ-di-3-methoxyphenyl*iso*propylamine (IV), however, was only obtained in poor yield : it was prepared by electrolytic reduction of the oxime of the ketone (V) and also by means

of the Hofmann reaction from the *amide* of the acid (VI). The main product of the latter reaction was a neutral nitrogenous substance, m. p. 135—136°, which is being further investigated by one of us (S. N. C.).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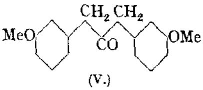
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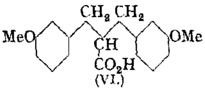
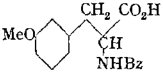
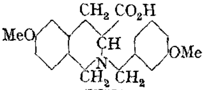
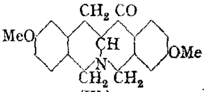

(VI.)

N-*Benzoyl*-β-3-*methoxyphenylalanine* (VII), required for the synthesis of 17-keto-3 : 12-dimethoxy-6 : 15 : 16 : 17-tetrahydroparaberine (IX), was prepared by hydrolysing the azlactone obtained from 3-methoxybenzaldehyde with dilute sodium hydroxide solution and reducing the product with sodium amalgam. Hydrolysis of (VII) with 10% hydrochloric acid gave β-3-*methoxyphenylalanine*, which was converted into 6-methoxy-2-3'-methoxybenzyl-1 : 2 : 3 : 4-tetrahydro*iso*quinoline-3-carboxylic acid (VIII) by two routes: (a) its formyl derivative was condensed with 3-methoxybenzyl chloride and the product, after the removal of the formyl group, was converted into (VIII) by means of formaldehyde; (b) it was converted into the *iso*quinoline derivative by means of formaldehyde and the 3-methoxybenzyl group then introduced.


(VII.)


(VIII.)


(IX.)

The acid (VIII) was cyclised by means of sulphuric acid to 17-keto-3 : 12-dimethoxy-6 : 15 : 16 : 17-tetrahydroparaberine (IX), which was isolated as the *semicarbazone* in a yield of about 15%.

The more difficult formation of (IX) compared with the ease of formation of the corresponding dimethoxytetrahydroprotoberberine (compare Chakravarti, Haworth, and Perkin, J., 1927, 2278; 1929, 196) points to the correctness of the conclusion of Campbell, Haworth, and Perkin (*loc. cit.*), although the types of final cyclisation involved are different and not strictly comparable.

The synthesis of 2 : 12-dimethoxytetrahydroparaberine is reserved for a future communication.

## Experimental.

dl-N-*Formyl*-β-*phenyl*-N-*benzylalanine*.—Benzyl chloride (4 g.) was added to a solution of *dl-N*-formyl-β-phenylalanine (5 g.) (Fischer and Schoeller, *Annalen*, 1907, **357**, 2) in methyl alcohol (20 c.c.), and the mixture refluxed for 4 hours on the water-bath. The alcohol was then removed, and the residue stirred with a little benzene. The dl-N-*formyl*-β-*phenyl*-N-*benzylalanine* obtained, after crystallising twice from methyl alcohol–ethyl acetate, formed clusters of colourless prisms (4·2 g.), m. p. 233° (Found: C, 72·1; H, 6·3. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·0%), easily soluble in water and alcohol, sparingly soluble in hot benzene and ethyl acetate, and almost insoluble in cold benzene and light petroleum.

dl-β-*Phenyl*-N-*benzylalanine*.—The preceding formyl derivative (3 g.) and 10% hydrochloric acid (100 c.c.) were heated together under reflux for 4 hours and then evaporated to dryness on a steam-bath. A solntion of the residue in the minimum amount of water was neutralised with ammonia and concentrated; dl-β-*phenyl*-N-*benzylalanine*, m. p. 222—225° (decomp.), separated (Found: N, 5·4. $C_{16}H_{17}O_2N$ requires N, 5·5%). It was readily soluble in water, but only very sparingly in the other usual organic solvents, and could be recrystallised from dilute alcohol. Attempts to convert it, by the action of (1) methylal and hydrochloric acid and (2) 40% formaldehyde in barium hydroxide solution, into the corresponding *iso*quinoline derivative in good yield were unsuccessful.

3-*Methoxyphenylacetonitrile*.—An alcoholic solution of 3-methoxybenzyl bromide (20·1 g.), prepared from hydrogen bromide and a benzene solution of the alcohol, and potassium cyanide (6·9 g.) were boiled together for 6 hours, the nitrile (15·2 g.), b. p. 160—165°/40 mm., being formed.

3 : 3'-*Dimethoxydibenzyl Ketone* (V).—(i) The reaction between 3-methoxybenzyl bromide

(20·1 g.) and magnesium (2·43 g.) in dry ether (60 c.c.) was started by addition of a little methyl iodide or iodine, and the mixture finally heated for 20 minutes on the water-bath with vigorous shaking. 3-Methoxyphenylacetonitrile (14·8 g.), dissolved in ether (50 c.c.), was gradually added, and the whole heated on the water-bath for 30 minutes and left overnight. The semi-solid mass was decomposed with dilute sulphuric acid and the products were isolated with ether and distilled under 10 mm., the following fractions being obtained: (a) Below 120°, 4·3 g., containing mainly the unchanged nitrile; (b) at 120—150°, 11·9 g., containing mainly the ketone (V), b. p. 135—145°/10 mm. after repeated distillation; (c) at 150—170°, 4·5 g.; (d) above 170°, 6·2 g. From fractions (c) and (d), by trituration with alcohol, a substance, m. p. 61—62°, was obtained which appeared to be 3 : 3'-*dimethoxydibenzyl* and could be readily crystallised from alcohol (Found: C, 79·3; H, 7·5. $C_{16}H_{18}O_2$ requires C, 79·4; H, 7·4%).

(ii) 3-Methoxyphenylacetic acid (1·66 g.), prepared by the hydrolysis of 3-methoxyphenylacetonitrile with methyl-alcoholic potash, was dissolved in alcohol (5 c.c.) and neutralised with 20% sodium hydroxide solution, phenolphthalein being used as the indicator. Thorium nitrate (1·38 g.) in water (10 c.c.) was stirred in, and the thorium 3-methoxyphenylacetate collected, washed with a little alcohol, and dried at 150° for 1 hour. The salt (11 g.) on destructive distillation gave 2·5 g. of an oil, from which a small quantity of 3 : 3'-dimethoxydibenzyl, m. p. 61—62°, separated on trituration with alcohol. The alcoholic filtrate contained mainly the ketone (V) [*semicarbazone*, m. p. 133° (Found: N, 13·0. $C_{18}H_{21}O_3N_3$ requires N, 12·8%); oxime, an oil].

The oxime (4·5 g.), when reduced electrolytically (cf. Kaplansky, *Ber.*, 1927, **60**, 1842), gave a very small amount of a base, which yielded a hydrochloride (0·15 g.), m. p. 169—170°, and formed an acetyl derivative, m. p. 94°, the analytical figures of which correspond to those of the *diacetyl* derivative of αγ-di-3-methoxyphenyl*iso*propylamine (Found: C, 70·8; H, 7·3. $C_{21}H_{25}O_4N$ requires C, 71·0; H, 7·0%).

*Di-3-methoxybenzylacetic Acid* (VI).—Ethyl sodiomalonate (sodium 4·6 g., absolute alcohol 75 c.c., and ethyl malonate 33 g.) was heated on the water-bath with 3-methoxybenzyl bromide (41 g.) for 3 hours, the alcohol removed, water added, and the product isolated with ether, treated with sodium (4·6 g.) dissolved in alcohol (75 c.c.), and refluxed with 3-methoxybenzyl bromide (41 g.) for 3 hours. The alcohol was then removed, and the product isolated with ether and distilled. The fraction (35 g.), b. p. 190—192°/16 mm., on hydrolysis with aqueous alcoholic potassium hydroxide yielded *di-3-methoxybenzylmalonic acid*, which crystallised from alcohol or chloroform in prisms, m. p. 185—186° (Found: C, 65·9; H, 5·7. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8%), readily soluble in alcohol and chloroform, sparingly soluble in water, benzene and ether, and almost insoluble in light petroleum. During the hydrolysis some di-3-methoxybenzylacetic acid (VI), m. p. 105°, was also formed, which was readily separated from the malonic acid by means of benzene, in which it was much more soluble.

The acid (VI), obtained in quantitative yield by heating the malonic acid at 210° for 15 minutes, crystallised from water in colourless prismatic needles, m. p. 105°. It formed a sparingly soluble *barium* salt (Found: Ba, 18·4. $C_{36}H_{38}O_8Ba$ requires Ba, 18·8%). Its ethyl ester had b. p. 150—153°/40 mm.

*Di-3-methoxybenzylacetamide*, prepared from the ester in the usual manner, crystallised from dilute methyl alcohol in long colourless needles, m. p. 102° (Found: N, 4·8. $C_{18}H_{21}O_3N$ requires N, 4·7%).

*α-Benzamido-3-methoxycinnamic Acid.*—The finely powdered azlactone (15 g., prepared from 3-methoxybenzaldehyde and hippuric acid) was heated with sodium hydroxide solution (3·3 g. in 1530 c.c. of water) on the steam-bath for 2—3 hours and the hot solution obtained was acidified. *α-Benzamido-3-methoxycinnamic acid* (14·2 g.), m. p. 178° (decomp.), separated in colourless crystals on cooling (Found: C, 68·6; H, 5·2; N, 4·4. $C_{17}H_{15}O_4N$ requires C, 68·7; H, 5·0; N, 4·7%). The acid was readily soluble in alcohol and chloroform, moderately soluble in hot benzene, and almost insoluble in light petroleum and cold water, and gave a sparingly soluble copper salt.

N-*Benzoyl-β-3-methoxyphenylalanine* (VII).—The above cinnamic acid (50 g.) was suspended in water (500 c.c.), and 2% sodium amalgam (520 g.) stirred in during 7 hours. When the solution was acidified, the *alanine* (VII), m. p. 144°, was precipitated; it was crystallised twice from methyl alcohol (Found: C, 68·0; H, 5·8; N, 4·7. $C_{17}H_{17}O_4N$ requires C, 68·2; H, 5·7; N, 4·7%).

*β-3-Methoxyphenylalanine.*—The alanine (VII) (10 g.) was heated under reflux with 10% hydrochloric acid (1250 c.c.) for 8 hours and the clear solution was concentrated to a small

volume, repeatedly extracted with benzene, and evaporated to dryness. The residue was dissolved in the minimum amount of water and neutralised with ammonia. β-3-*Methoxyphenylalanine* slowly separated; it crystallised from dilute alcohol in needles, m. p. 215° (decomp.) (Found: C, 61·4; H, 6·9; N, 7·0. $C_{10}H_{13}O_3N$ requires C, 61·5; H, 6·7; N, 7·2%). Yield, more than 90%.

N-*Formyl*-β-3-*methoxyphenyl*-N-3′-*methoxybenzylalanine*.—β-3-Methoxyphenylalanine (5 g.) and formic acid (3 c.c.) were warmed gently for 1 hour on the water-bath, and the excess of formic acid removed under diminished pressure. The residual semi-solid was heated for 2 hours on the steam-bath and crystallised from ethyl acetate, the formyl derivative being obtained in small prisms, m. p. 156°, readily soluble in hot water and alcohol and only sparingly in benzene. This (2 g.) and 3-methoxybenzyl chloride (2·5 g.) were refluxed together for 6 hours in methyl-alcoholic solution. The alcohol was removed, the residue stirred with benzene, and the solid which separated was crystallised from ethyl acetate, N-*formyl*-β-3-*methoxyphenyl*-N-3′-*methoxybenzylalanine* being obtained in plates, m. p. 186—188° (Found: C, 66·5; H, 6·2. $C_{19}H_{21}O_5N$ requires C, 66·5; H, 6·1%), very sparingly soluble in acetone and benzene, moderately soluble in ethyl acetate and water, and easily soluble in alcohol.

β-3-*Methoxyphenyl*-N-3′-*methoxybenzylalanine*.—The preceding formyl compound (1 g.) and 10% hydrochloric acid (100 c.c.) were heated under reflux for 4 hours, and the solution evaporated to dryness. The residue was dissolved in the minimum amount of water, and the solution made just alkaline with ammonia and concentrated on the water-bath; β-3-*methoxyphenyl*-N-3′-*methoxybenzylalanine*, m. p. 233°, which separated, was crystallised from hot water (Found: C, 68·5; H, 6·8. $C_{18}H_{21}O_4N$ requires C, 68·6; H, 6·7%).

6-*Methoxy*-2-3′-*methoxybenzyl*-1 : 2 : 3 : 4-*tetrahydro*iso*quinoline*-3-*carboxylic Acid* (VIII).—The above alanine (1 g.), dissolved in a slight excess of barium hydroxide solution, was treated with formaldehyde (5 c.c. of 40%) with vigorous shaking. The precipitate was dissolved in 25% hydrochloric acid (30 c.c.), and the solution evaporated to dryness on a steam-bath. The residue was made just alkaline with ammonia and boiled to remove the excess. The brown precipitate obtained was extracted several times with water, and the combined extracts concentrated to a small volume; the acid (VIII), m. p. 223—225°, then separated. Its *barium* salt was sparingly soluble and crystallised well (Found: Ba, 17·8. $C_{38}H_{40}O_8N_2Ba$ requires Ba, 17·5%).

6-*Methoxy*-1 : 2 : 3 : 4-*tetrahydro*iso*quinoline*-3-*carboxylic Acid*.—β-3-Methoxyphenylalanine (3 g.), dissolved in barium hydroxide solution, was shaken with 40% formaldehyde (8 c.c.) and the precipitate was collected, washed several times with methyl alcohol, and warmed with concentrated hydrochloric acid (40 c.c.) on the steam-bath for 25 minutes. The clear solution was evaporated almost to dryness, and the residue just neutralised with ammonia; 6-*methoxy*-1 : 2 : 3 : 4-*tetrahydro*iso*quinoline*-3-*carboxylic acid* separated as a pale brown powder which, recrystallised from water, formed colourless plates, m. p. 263—264° (decomp.) (Found: N, 7·0. $C_{11}H_{13}O_3N$ requires N, 6·8%). When heated with 3-methoxybenzyl chloride and sodium acetate in alcoholic solution for 5 hours, it gave 6-methoxy-*N*-3′-methoxybenzyl-1 : 2 : 3 : 4-tetrahydro*iso*quinoline-3-carboxylic acid (VIII).

*Semicarbazone of* 17-*Keto*-3 : 12-*dimethoxy*-6 : 15 : 16 : 17-*tetrahydroparaberine*.—The acid (VIII) (2 g.) was warmed on the water-bath for 20 minutes with 70% sulphuric acid (7 c.c.), the product poured into cold water, and the filtered solution basified and extracted with chloroform (five times). Evaporation of the dried extract left a residue, which was converted into the *semicarbazone*; this separated from methyl alcohol as a colourless crystalline powder (0·31 g.), m. p. 250—252° (decomp.) (Found: N, 15·5. $C_{20}H_{22}O_3N_4$ requires N, 15·3%).

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## 30. *The Action of the Oppenauer Reagent on Primary Alcohols, including Vitamin-A.*

By J. W. Batty, A. Burawoy, S. H. Harper, I. M. Heilbron, and W. E. Jones.

**Attempts to obtain the aldehyde corresponding to vitamin-A by the oxidation of the latter with aluminium *tert.*-butoxide in the presence of acetone have resulted in the isolation of a ketone, $C_{23}H_{32}O$, characterised by a semicarbazone, m. p. 193°, a**

*p*-tolylsemicarbazone, m. p. 217—218°, and a *p*-chlorobenzoylhydrazone, m. p. 198—199°. That this ketone is a secondary condensation product of the originally produced vitamin-A aldehyde with acetone has been established by a series of analogous reactions, *viz.*, oxidation of geraniol to ψ-ionone, cinnamyl alcohol to cinnamylideneacetone, benzyl alcohol to benzylideneacetone, and furfuryl alcohol to furfurylideneacetone. As neither tetrahydrogeraniol, β-phenylethyl alcohol, nor γ-phenylpropyl alcohol undergoes oxidation under these conditions, it would appear that the reaction is specific, in the case of primary alcohols, for those containing an activated hydroxyl group.

Holmes and Corbet (*J. Amer. Chem. Soc.*, 1937, **59**, 2042) have described the preparation of crystalline vitamin-A and while it would appear that spectroscopically this material is virtually pure ($\varepsilon_{max.}$ = 60,000), the low melting point (7·5—8°) would seem to indicate that it is a mixture of geometrical isomers [cf. δ-(2 : 2 : 6-trimethyl-$\Delta^{6}$-*cyclo*hexenyl)-β-methyl-$\Delta^{\alpha\gamma}$-butadiene-α-carboxylic acid; Karrer, Salomon, Morf, and Walker, *Helv. Chim. Acta*, 1932, **15**, 878]. This view, that vitamin-A (I), when obtained as a single entity free from geometrical isomers, will have a moderately high melting point, is based on the facts that the polyene aliphatic alcohols are high-melting solids ($\Delta^{\beta\delta\zeta}$-octatrien-α-ol, m. p. 100°; γη-dimethyl-$\Delta^{\beta\delta\zeta}$-octatrien-α-ol, m. p. 46—47°; $\Delta^{\beta\delta\zeta\theta}$-decatetraen-α-ol, m. p. 122—124°; $\Delta^{\beta\delta\zeta\theta\kappa}$-dodecapentaen-α-ol, m. p. 204°; and γηλ-trimethyl-$\Delta^{\beta\delta\zeta\theta\kappa}$-dodecapentaen-α-ol, m. p. 136—137°) and that even β-*cyclo*geraniol (II) has a melting point of 43—44° (Kuhn and Hoffer, *Ber.*, 1934, **67**, 357). We have ourselves made many attempts, using rich vitamin-A concentrates prepared from halibut liver-oil, to obtain the vitamin in crystalline form, but have never met with the success achieved by Holmes and Corbet (*loc. cit.*), nor have we been more fortunate in our efforts to obtain a crystalline derivative by the method of Hamano (*Sci. Papers Inst. Phys. Chem. Research, Tokyo*, 1935, **28**, 69; 1937, **32**, 44), who claims to have prepared a β-naphthoate, m. p. 76°, and an anthraquinone-2-carboxylate, m. p. 124°.

In view of our unpromising results, we turned our attention to the possibility of converting the vitamin into its corresponding aldehyde (III), from which we hoped, after its purification *via* a suitable crystalline derivative, to regenerate the pure vitamin by reduction with aluminium *iso*propoxide. Oppenauer (*Rec. trav. chim.*, 1937, **56**, 141) has described an elegant method of oxidising secondary alcohols, *e.g.*, ergosterol, to the corresponding ketones by refluxing with aluminium *tert.*-butoxide in benzene solution in the presence of a large excess of acetone as hydrogen acceptor; in view of the mild conditions employed, we have investigated the application of this reaction to vitamin-A and other primary alcohols.

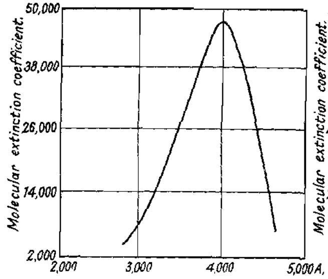
It was found that oxidation of a rich vitamin-A concentrate ($E^{1\%}_{1cm.}$ 3280 A. = 1300)* under these conditions gave a crude product exhibiting a new absorption band at 4010 A. ($E^{1\%}_{1cm.}$ = 950) together with that at 3280 A. due to unchanged vitamin-A ($E^{1\%}_{1cm.}$ = 300). After successive purifications by chromatographic adsorption on alumina and by treatment with the Girard Reagent P (Girard and Sandulesco, *Helv. Chim. Acta*, 1936, **19**, 1095), a carbonyl compound was isolated exhibiting a single well-defined absorption maximum at 4010 A., the extinction coefficient ($E^{1\%}_{1cm.}$ = 1450) of which remained unchanged after distillation in high vacuum. The compound formed a ***semicarbazone***, m. p. 193°, a p-***tolylsemicarbazone***, m. p. 217—218°, and a p-***chlorobenzoylhydrazone***, m. p. 198—199°, the analyses of which revealed that they were derived, not from the anticipated aldehyde $C_{20}H_{28}O$, but from a substance of molecular formula $C_{23}H_{32}O$. The

| Compound. | Solvent. | $\lambda_{max.}$, A. | $\varepsilon_{max.}$ |
|---|---|---|---|
| (a) Carbonyl compound | EtOH | 4010 | 48,900 |
| (b) Semicarbazone of (a) | EtOH | 3970 | 86,100 |
| (c) *p*-Tolylsemicarbazone of (a) | $CHCl_3$ | 4140 | 84,200 |
| (d) *p*-Chlorobenzoylhydrazone of (a) | $CHCl_3$ | 4135 | 80,800 |

* $E^{1\%}_{1cm.}$ is defined as the extinction coefficient ($\log I_0/I$) of a 1 cm. layer of a 1% solution of a substance at a particular wave-length, $I_0$ being the intensity of the light incident on the solution, and $I$ the intensity of the transmitted light.

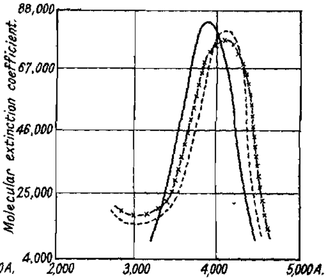
only feasible explanation of the production of such a compound is that it is the ketone (IV), formed by the subsequent condensation of the initially produced vitamin-A aldehyde with the acetone present. This is strongly supported by the spectrographic data (Table; Figs. 1 and 2), since the position of the absorption maximum of the carbonyl compound (4010 A.) lies mid-way between those of α-aldehydo-$\Delta^{\alpha\gamma\epsilon\eta\iota}$-undecapentaene (V) and α-aldehydo-$\Delta^{\alpha\gamma\epsilon\eta\iota\lambda\nu}$-pentadecaheptaene (VI), which absorb respectively at 3850 A. and 4120 A. (unpublished work).

FIG. 1.



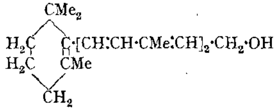

$C_{23}$ *Ketone* (IV) *in* EtOH.

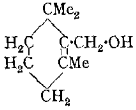
FIG. 2.

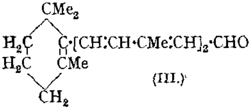


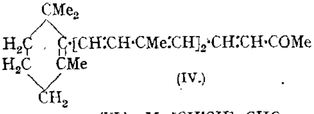

——— *Semicarbazone of* (IV) *in* EtOH.
– – – – p-*Tolylsemicarbazone of* (IV) *in* $CHCl_3$.
–×–× p-*Chlorobenzoylhydrazone of* (IV) *in* $CHCl_3$.

With a view to establishing the validity of this suggested reaction mechanism, the action of the Oppenauer reagent upon a selection of other primary alcohols was next investigated. We have found that, whereas geraniol gives a good yield of ψ-ionone and

(I.) 

 (II.)

 (III.)

 (IV.)

(V.) $Me\cdot[CH:CH]_5\cdot CHO$ (VI.) $Me\cdot[CH:CH]_7\cdot CHO$

cinnamyl, furfuryl and benzyl alcohols give respectively cinnamylidene-, furfurylidene-, and benzylidene-acetone, tetrahydrogeraniol, β-phenylethyl alcohol, and γ-phenylpropyl alcohol on the other hand are completely unreactive. It thus follows that, at any rate in the case of primary alcohols, an activating centre, such as an αβ-double bond or an aromatic nucleus contiguous to the $CH_2\cdot OH$ group, is necessary for oxidation to proceed.

While in none of the cases cited has it been possible to determine whether the aldehyde exists as such during the reaction, the ability of aluminium *tert.*-butoxide to effect condensation has been established by the conversion of citral into ψ-ionone by condensation with acetone under the standard conditions.

With the object of avoiding the complications due to the presence of the acetone, the reaction is now being studied with other ketones, such as diisopropyl ketone, which contain no reactive methylene groups.

## Experimental.

*Oxidation of Vitamin-A.*—A solution of a vitamin-A concentrate (18·5 g., $E^{1\%}_{1cm.}$ 3280 A. = 1300) in a mixture of dry A.R. benzene (500 c.c.) and acetone (200 c.c., distilled from potassium permanganate and dried over potassium carbonate) was refluxed on the steam-bath in a stream of nitrogen for 30 hours together with freshly prepared aluminium *tert.*-butoxide (20 g.). The deep red suspension was diluted with water and filtered; the benzene layer was removed, washed with water, and dried over sodium sulphate. After removal of solvent under reduced pressure the residual red viscous oil was dissolved in light petroleum and adsorbed on a column of alumina. The dark reddish-brown zone, which passed slowly down the column on washing with solvent, was elutriated with light petroleum–methyl alcohol, and the elutriate washed with water and dried. After removal of solvent the product, which still contained vitamin-A, was dissolved in a mixture of absolute alcohol (200 c.c.) and glacial acetic acid (20 c.c.) and refluxed with Girard Reagent P (20 g.) for 1 hour. The whole was poured into water and, after neutralisation of 90% of the acetic acid with sodium bicarbonate, was repeatedly extracted with ether. The aqueous layer was warmed at 50—60° for ½ hour with a saturated solution of oxalic acid (20 g.), and the regenerated ketone extracted with ether. After removal of solvent from the washed and dried solution, the residual deep red oil was distilled in a high vacuum (bath temp. 135°, $10^{-4}$ mm.), giving *β-keto-μ-(2 : 2 : 6-trimethyl-$\Delta^{6}$-cyclohexenyl)-ζκ-dimethyl-$\Delta^{\gamma\epsilon\eta\kappa\lambda}$-dodecapentaene* (IV) as a viscous orange-yellow oil which resisted all attempts at crystallisation. The ketone was characterised by a well-defined absorption maximum at 4010 A. ($E^{1\%}_{1cm.}$ = 1450) and with chloroformic antimony trichloride gave a blue-green colour with a maximum at 6460 A. (Found : C, 84·8; H, 9·6. $C_{23}H_{32}O$ requires C, 85·2; H, 9·9. Calc. for $C_{20}H_{28}O$ : C, 84·5; H, 9·9%). The *semicarbazone*, prepared in the normal manner, crystallised from aqueous acetone in pale yellow micro-needles, m. p. 193° (Found : C, 75·6; H, 9·0; N, 11·2. $C_{24}H_{35}ON_3$ requires C, 75·6; H, 9·2; N, 11·0. Calc. for $C_{21}H_{31}ON_3$ : C, 73·9; H, 9·1; N, 12·3%). The *p-tolylsemicarbazone* was prepared by heating a solution of the ketone (1·1 g.) in alcohol (30 c.c.), containing a few drops of glacial acetic acid, with *p*-tolylsemicarbazide acetate (0·8 g.) on the steam-bath for 10 minutes. The product, which separated on cooling, crystallised from ethyl acetate in golden-yellow needles, m. p. 217—218° (Found : C, 78·7; H, 8·6; N, 8·8. $C_{31}H_{41}ON_3$ requires C, 78·9; H, 8·7; N, 8·9. Calc. for $C_{28}H_{37}ON_3$ : C, 77·9; H, 8·6; N, 9·7%). The *p-chlorobenzoylhydrazone* was obtained by refluxing the ketone (2 g.) with *p*-chlorobenzoylhydrazine (1 g.) in alcohol (15 c.c.), containing two drops of glacial acetic acid, for 1 hour. The product which separated from the hot solution crystallised from ethyl acetate in orange-red micro-crystals, m. p. 198—199° (Found : C, 75·3; H, 7·8; N, 5·9; Cl, 7·1. $C_{30}H_{37}ON_2Cl$ requires C, 75·5; H, 7·8; N, 5·9; Cl, 7·4. Calc. for $C_{27}H_{33}ON_2Cl$ : C, 74·2; H, 7·6; N, 6·4; Cl, 8·1%).

*Oxidation of Geraniol.*—Geraniol (14 g.) was oxidised with aluminium *tert.*-butoxide (20 g.) in a mixture of acetone (200 c.c.) and benzene (500 c.c.) for 30 hours exactly as described above for vitamin-A. The crude product on distillation gave a main fraction, b. p. 155—165°/23 mm., consisting of almost pure ψ-ionone as shown by its absorption maximum at 2910 A. ($\varepsilon_{max.}$ = 22,800) in alcohol. Yield, 70%. The 2 : 4-dinitrophenylhydrazone, m. p. 141°, showed no depression in melting point on admixture with an authentic specimen.

*Condensation of Citral with Acetone.*—A solution of aluminium *tert.*-butoxide (20 g.) in a mixture of acetone (200 c.c.) and dry benzene (500 c.c.) was refluxed with citral (15 g.) for 30 hours. After dilution with water, filtration from alumina, and removal of the solvent from the dried benzene solution, distillation of the residue gave a 75% yield of ψ-ionone, b. p. 150—163°/25 mm., identified as above.

*Cinnamylideneacetone.*—Cinnamyl alcohol (10 g.) was oxidised with aluminium *tert.*-butoxide (20 g.) in a mixture of benzene (500 c.c.) and acetone (200 c.c.) for 24 hours at 90—95°. Distillation of the crude product gave two fractions : (a) b. p. 130—160°/20 mm. (2·1 g.), which did not solidify at 0°, and (b) b. p. 160—180°/20 mm. (6·2 g.). The solid which separated on cooling was freed from oil by pressure between porous tiles and crystallised from light petroleum (b. p. 40—60°), giving cinnamylideneacetone in pale yellow prisms, m. p. 68° (Diehl and Einhorn, *Ber.*, 1885, **18**, 2322, give m. p. 68°). For further characterisation the ketone was converted into its oxime, which crystallised from aqueous alcohol in needles, m. p. 152°.

*Furfurylideneacetone.*—Furfuryl alcohol (16 g.) was oxidised with aluminium *tert.*-butoxide (10 g.) in acetone (100 c.c.) and benzene (250 c.c.) as above for 24 hours. Distillation of the product gave a fraction (3·3 g.), b. p. 140—150°/50 mm., which solidified on cooling (m. p.

37—38°) and showed no depression in melting point on admixture with authentic furfurylideneacetone, m. p. 39°. Its phenylhydrazone, prepared in alcoholic acetic acid, crystallised from alcohol in yellow needles, m. p. 128—129°, no depression in melting point being observed on admixture with a specimen of furfurylideneacetonephenylhydrazone, m. p. 131°.

*Benzylideneacetone.*—Benzyl alcohol (8 g.) was oxidised by the standard method with aluminium *tert.*-butoxide (10 g.) in acetone (100 c.c.) and benzene (250 c.c.) for 24 hours. Distillation of the product gave two fractions: (a) b. p. 80—140°/25 mm. (2 g.); (b) b. p. 142—150°/25 mm. (3 g.). The latter, which solidified on standing to colourless plates, m. p. 40°, was characterised as benzylideneacetone by conversion into its oxime, m. p. 115° (Marshall, J., 1915, **107**, 521, gives m. p. 116°).

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The University, Manchester. [*Received, November 20th, 1937.*]

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## 31. *The Kinetics of Iodine Addition to Olefinic Compounds.*

By N. J. Bythell and P. W. Robertson.

In a recent investigation on the kinetics of bromine addition it was shown that the reactions in acetic acid were termolecular; in carbon tetrachloride they took place predominantly on a surface film, which was relatively stable within definite concentration–temperature limits characteristic for the adsorbed substance. It is now found that iodine addition follows a similar course, being termolecular with low heats of activation in the dissociating solvents nitrobenzene and acetic acid, heterogeneous in the non-polar media carbon tetrachloride and hexane. Certain constitutive influences are now noted under definitely non-heterogeneous conditions, and found to be in accordance with electronic conceptions.

The surface reactions between iodine and compounds such as allyl alcohol and undecenoic acid are unexpectedly rapid, and it seems necessary to assume a suddenly enhanced activation of the molecules at the moment of impact.

In comparison with the extensive researches on bromine addition, there has been relatively little work on iodine addition in organic solvents. Such investigations are troublesome, being for the most part very slow, and disturbed by the incidence of a reverse reaction, which is catalysed by iodine. Herz and Mylius (*Ber.*, 1907, **40**, 2898) found in the reaction of allyl alcohol with iodine, in carbon tetrachloride, chloroform, and carbon disulphide, that bimolecular constants were obtained in the individual experiments, but they varied considerably with the concentration. The results of Meyer and Pukall (*Z. physikal. Chem.*, 1929, **145**, 360) showed similar discrepancies. Schumacher (*J. Amer. Chem. Soc.*, 1930, **52**, 3132) concluded that the reaction $C_2H_4 + I_2$ in carbon tetrachloride was homogeneous, proceeding by a chain mechanism.

The investigation by Caughley and Robertson (J., 1933, 1323) was designed more especially to examine the equilibria set up between iodine, allyl alcohol, and its addition product. The reactions appeared bimolecular, and it was unexpectedly found, although not explained at the time, that in a series of non-dissociating solvents there were very considerable differences in rate: benzene ($k_2 = 0{\cdot}01$); toluene ($k_2 = 0{\cdot}02$); carbon tetrachloride ($k_2 = 0{\cdot}07$); hexane ($k_2 = 2{\cdot}1$). An investigation of the conditions determining bromine addition (Robertson, Clare, McNaught, and Paul, J., 1937, 335) revealed that the reactions in a solvent like carbon tetrachloride with low internal pressure were heterogeneous, taking place largely on activated surface films. It is significant, therefore, that the $k_2$ values quoted above are in the inverse order of the internal pressures of the solvents. It was further shown that bromine addition in a dissociating solvent such as acetic acid was a termolecular reaction with a very low heat of activation, two molecules of bromine participating for each molecule of unsaturated compound.

In the light of these results a more detailed examination of iodine addition in a range of solvents has been undertaken. With concentrations of the order M/50, the equilibria for

allyl compounds are in the region corresponding with 50% iodine absorption. By having the unsaturated compound in excess (A = M/2, $I_2$ = M/50), the equilibria are shifted to a region with 95% absorption. The back reactions thus become practically negligible under these conditions over the first 50% of the iodine absorption. There is further the very important advantage that the velocities are greatly increased, thus allowing the necessary data to be much more expeditiously collected.

*The Homogeneous Reactions.*—Iodine additions in acetic acid and nitrobenzene are termolecular; the compounds examined were allyl alcohol, its acetate, benzoate, and bromide, and undecenoic acid. This is evident from the following considerations :

(1) With the unsaturated compound in excess, constant pseudo-bimolecular values $k_2$ are obtained, as illustrated by the following typical results :

| | | | | | |
|---|---|---|---|---|---|
| Iodine consumed, % ($x$) | 10 | 20 | 30 | 40 | 50 |
| Allyl alcohol in $PhNO_2$ ($I_2$ = M/50, A = M/2), 25° | 2·9 | 3·0 | 3·1 | 3·0 | 3·1 |
| ,, ,, ($I_2$ = M/100, A = M/4), 25° | 1·5 | 1·5 | 1·5 | 1·6 | 1·6 |
| Undecenoic acid in HOAc ($I_2$ = M/50, A = M/2), 13° | 2·4 | 2·4 | 2·4 | 2·4 | 2·3 |
| ,, ,, ,, ,, 45° | 3·7 | 3·8 | 3·8 | 3·9 | 4·1 |

(2) By halving the concentrations of both reactants the $k_2$ values are halved and the times for the same percentage change reduced to a quarter, in accordance with the theoretical expectation, as illustrated above for allyl alcohol.

(3) With the reactants, $I_2$ = M/40, A = M/80 and $I_2$ = M/80, A = M/40, the initial rate at $x$ = 10%, *i.e.*, before the back reaction is appreciable, is greater when the iodine is in excess.

The iodine additions therefore correspond with the bromine additions, and like them, are also characterised by low heats of activation. The following $k_2$ values ($I_2$ = M/50, A = M/2) were obtained at different temperatures.

| | | 14·4°. | 25°. | 35°. | 45°. | 55°. | $E$. | $B \times 10^{-3}$. |
|---|---|---|---|---|---|---|---|---|
| Allyl acetate in HOAc | $k$ | — | 0·085 | 0·13 | 0·17 | 0·22 | 6,100 | 19 |
| | ($k$) | — | 0·090 | 0·12 | 0·17 | 0·23 | | |
| Allyl alcohol in HOAc* | $k$ | — | 0·21 | 0·29 | 0·35 | 0·46 | 4,800 | 5·2 |
| | ($k$) | — | 0·21 | 0·28 | 0·36 | 0·45 | | |
| Allyl alcohol in $PhNO_2$ | $k$ | 2·54 | 3·06 | — | 4·44 | — | 3,300 | 6·2 |
| | ($k$) | 2·50 | 3·10 | — | 4·38 | — | | |

* F. p. measurements under similar conditions indicated no esterification.

The values denoted by ($k$) are obtained from the straight-line log $k$–$1/T$ curve, and $E$ is calculated graphically. To obtain the $B$ parameters in the Arrhenius equation, $k_3 = Be^{-E/RT}$, the values of $k_3$ were obtained from the expression $k_2 = bk_3/4$, since rate = $k_3(b - x)\,[(a - x)/2]^2$, and $x$ is small in comparison with $b$, the concentration of the component in excess. With increase in the rate of iodine addition there is a reduction of $E$. The $B$ parameters in the corresponding bromine additions, which proceed $10^4$ times as fast, are in the region $10^5$ (l. g.-mol.$^{-1}$min.$^{-1}$).

The following table shows the effect of solvent on the rate of iodine addition. For the purposes of comparison pseudo-bimolecular $k_2$ values are given (A = M/2, $I_2$ = M/50), although the reactions in the non-polar solvents do not proceed by this mechanism.

| Solvent | $PhNO_2$ | HOAc | PhCl | $CCl_4$ | $C_6H_{14}$ |
|---|---|---|---|---|---|
| Allyl alcohol, $k_2$ (25°) | 3·1 | 0·22 | 0·41 | 0·41 | 0·65 |
| Allyl acetate, $k_2$ (25°) | 0·94 | 0·088 | 0·040 | 0·006 | 0·009 |

*The Heterogeneous Reactions.*—Whereas iodine additions in nitrobenzene and acetic acid, which form brown solutions, are homogeneous and termolecular, those in chlorobenzene, carbon tetrachloride, and hexane (*i.e.*, the violet solutions) are heterogeneous. This conclusion is reached as a result of the following observations: (1) When the reaction vessel is packed with glass beads, the reaction proceeds more rapidly, and this increase may be very considerable; for instance, in the reaction between M/40-iodine and M/40-allyl alcohol in hexane at 25°, the rate was increased 15-fold. Such "packing" not only enlarges the surface area, but also decreases the average striking distance of the molecules from the surface. (2) On reducing the concentrations of the reactants, a region is reached where there is a rapid diminution in velocity. Similar observations were made with reference to bromine addition,

and it was concluded that for a given solvent at each temperature there is a limiting concentration below which the surface film becomes unstable :

Iodine and allyl alcohol, both M/100; $k_2$ (25°) = 0·058; both M/200, $k_2$ (25°) = 0·004.
Iodine and undecenoic acid, both M/50; $k_2$(25°) = 0·070; both M/100, $k_2$(25°) = 0·011.

(3) Similarly there is a limiting temperature, above which the adsorbed film becomes unstable with a rapid diminution in reaction rate: For M/100-iodine and -allyl alcohol, $k_2$(25°) = 0·058; $k_2$(35°) = 0·0009.

With the unsaturated compound in excess the heterogeneous effects are modified owing to its preferential adsorption; and this is reflected in the smaller differences in rate with different solvents. Thus at 25° :

$I_2$ = M/40, allyl alcohol = M/40; $k_2$ ($CCl_4$) = 0·0012; $k_2$ ($C_6H_{14}$) = 0·036.
$I_2$ = M/40, allyl alcohol = M/2; $k_2$ ($CCl_4$) = 0·41; $k_2$ ($C_6H_{14}$) = 0·65.

With the organic component in excess, constant pseudo-unimolecular values, $k_1$, are obtained when the relative adsorption is considerable. Thus for allyl alcohol at 25° :

| Iodine consumed, % ($x$) | 10 | 20 | 30 | 40 | 50 | 60 | 70 |
|---|---|---|---|---|---|---|---|
| In $C_6H_{14}$; $I_2$ = M/50, A = M/2 | 0·008 | 0·010 | 0·011 | 0·012 | 0·012 | 0·013 | 0·012 |
| In $C_6H_{14}$; $I_2$ = M/100, A = M/2 | 0·0031 | 0·0029 | 0·0029 | 0·0030 | 0·0031 | 0·0032 | 0·0032 |
| In $CCl_4$; $I_2$ = M/50, A = M/2 | 0·0070 | 0·0069 | 0·0067 | 0·0067 | 0·0069 | 0·0069 | 0·0068 |

This constancy of $k_1$ may be, however, in part accidental. The decrease in volume of the solvent under the experimental conditions increases the surface–volume ratio; the resultant increase in $k_1$ must consequently be offset by a slight decrease in the activity of the surface film.

Whereas the relative rate of iodine addition to allyl alcohol and allyl acetate in dissociating solvents is 3 : 1, yet in carbon tetrachloride and hexane it is 100 : 1. The relative rate of the heterogeneous reactions will depend on (*a*) the density of the surface film, the number of molecules per unit area, (*b*) the effectiveness of the impacts on this film, and such effects may not at present be distinguished. For allyl alcohol this total effect is relatively so great that the temperature coefficient, although irregular, is positive; for allyl acetate, however, under the same conditions, it is negative.

The adsorption effect for allyl alcohol in hexane is so considerable that iodine addition is more rapid in this solvent than in acetic acid. Halogen addition is determined by the polarity of the halogen molecule, bromine chloride, for example, reacting more rapidly than bromine, and this causes the initial attack by the positive halogen atom. In the brown iodine solutions such polarity may be enhanced by the formation of complexes, $XO \rightarrow I\!-\!I$. The high reactivity of iodine in the violet solutions is consequently unexpected, since in such solvents as benzene and carbon tetrachloride iodine is completely non-polar (*Nature*, 1935, **135**, 71). It must therefore be assumed that the iodine molecule becomes polarised immediately prior to addition, by an impact with the surface film. Such an effect might be more considerable with the hydroxyl group than with the less strongly polar acetoxy-group, and the heterogeneous rates thus correspondingly influenced.

*Constitution and Iodine Addition.*—A general examination, in terms of the electronic theory, of the conditions determining the rate of halogen addition has been made by Ingold and Ingold (J., 1931, 2354). In brief, their theory states that the ease of addition is dependent, not so much upon the induced polarity of the ethylene carbon atoms, as upon the electronic condition of the ethylene system as a whole. This acts in a sense as an electron sink; electron accession to it will favour, and electron regression from it will hinder, halogen addition. Accordingly, the methyl group will have an accelerating, and carboxyl group a retarding, influence, the electromeric effect here acting in the same sense as the inductive effect; with bromine these two influences act reversely, but the inductive effect for this type of reaction is more powerful, so that bromine attached to an ethylene carbon will reduce the rate of halogen addition. To test these theoretical conclusions, we carried out experiments on the relative rates of bromine addition to various compounds in dichloromethane at −35°. Actually, the conditions, *viz.*, low temperature and solvent

of small internal pressure, even if hydrogen bromide is present (Ingold and Anantakrishnan, J., 1935, 984), favour heterogeneous reactions, and the rates of addition may be influenced by factors other than those theoretically considered. For instance, whereas allyl acetate and allyl benzoate add bromine at the same rate in acetic acid solution, the heterogeneous rates in carbon tetrachloride are in the ratio 100 : 1. Similarly, allyl alcohol and allyl acetate add iodine in dissociating solvents in the ratio 3 : 1, and in hexane in the ratio 70 : 1.

The iodine additions with certain typical compounds now to be considered have been carried out under conditions where heterogeneous disturbances are absent, and the following relative rates have been obtained from a comparison of the pseudo-bimolecular $k_2$ values: $CH_2{:}CH_2$ (0·10), $CH_2{:}CH{\cdot}CH_3$ (1), $CH_2{:}CH{\cdot}[CH_2]_8{\cdot}CO_2H$ (3), $CH_2{:}CH{\cdot}CH_2{\cdot}OH$ (0·28), $CH_2{:}CH{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}CH_3$ (0·078), $CH_2{:}CH{\cdot}O{\cdot}COPh$ (0·067), $CH_2{:}CH{\cdot}CH_2Br$ (0·028).

These results are in accordance with the theory of Ingold and Ingold. The methyl group has an accelerating influence, and the effect is greater with $[CH_2]_8{\cdot}CO_2H$, which acts as an alkyl, the distant carboxyl group being negligible. The hydroxyl group and the bromine atom reduce the rate when substituted in propylene, and the electron-absorbing groups acetyl and benzoyl cause the allyl esters to be less reactive than allyl alcohol. One exception, however, has been noted; allyl iodide, which might be expected to have a reaction rate of the same order as allyl bromide, does not add iodine in acetic acid solution. This may be due to the instability of the ion formed at the first stage of the addition; $CH_2I{-}\overset{\oplus}{C}H{-}CH_2I$, owing to the presence of two iodine atoms with their relatively loosely held electrons, breaks up immediately into allyl iodide and the positive iodine ion. Allyl iodide with bromine, it may be noted, reacts rapidly at first, but the reaction then slows down very considerably, reaching an equilibrium: this is possibly due to a similar change, $CH_2Br{-}\overset{\oplus}{C}H{-}CH_2I \longrightarrow CH_2Br{\cdot}CH{=}CH_2 + \overset{\oplus}{I}$.

The tentative suggestion is made that the rapid surface reactions discussed above are possibly simple prototypes of the reactions taking place on the surface of the living cell. These similarly indicate a high effectiveness of impact; they show also a falling off in rate at higher temperatures; and they increase suddenly in rate above a certain limiting concentration of reactant, as appears for example in the action of certain hormones.

## EXPERIMENTAL.

The reacting compounds and solvents were as described in previous communications (J., 1933, 1323; 1937, 335). The nitrobenzene (Merck), m. p. 5·35°, was unaffected in solvent activity after fractionation. The hexane, after being left for 24 hours with 96% sulphuric acid, had b. p. 67·5—68·5°/750 mm. The ethylene and propylene, prepared by the phosphoric acid method (Newth, J., 1901, 79, 915) and purified by ice-cooling and passage over potassium hydroxide and calcium chloride, were absorbed in acetic acid–carbon tetrachloride (1 : 1), the ethylene not being sufficiently soluble in pure acetic acid. Independent experiments had shown that the reactions in this mixed solvent were not heterogeneous. The strengths of these solutions were determined with Wijs's reagent and diluted accordingly. The velocity ratio of ethylene to propylene was thus determined; the latter was compared with allyl alcohol in this same solvent, and the relative velocities of the various compounds obtained.

The titrations were carried out as previously described; the values of $k$ obtained from the smoothed curves are in l./g.-mol.-min. In the nitrobenzene experiments it was necessary to add some substance such as ether before titration. Most of the significant results have already been quoted in the text. When $k_2$ values are quoted for the heterogeneous reactions to show comparative rates, the $x = 20\%$ values are given.

For certain of the reactions in acetic acid and nitrobenzene the equilibria were examined, and found not to conform with the simple equation, $I_2 + A \rightleftarrows AI_2$. This is due in part to the termolecular flature of the forward reaction, and in part to the catalytic influence of iodine on the reverse reaction. The dissociation of ethylene di-iodide in carbon tetrachloride has been examined by Polissar (*J. Amer. Chem. Soc.*, 1930, **52**, 956) and found to be autocatalytic. Similarly, measurements of the dissociation of the addition compounds of allyl alcohol and iodine, and allyl acetate and iodine, were found (experiments of F. G. Caughley and J. L. Mandeno) to give rising $k_1$ values in alcoholic solution, whereas $k_1$ would be expected normally to fall owing to the incidence of the reverse reaction.

The effect of water on the rate of iodine addition in acetic acid has also been examined. The following values, for A = M/2, $I_2$ = M/40, were obtained at 25°:

| | | | | |
|---|---|---|---|---|
| $H_2O$, % | 0 | 5 | 10 | 15 |
| $k_2$ | 0·21 | 0·49 | 0·84 | 1·4 |

For the corresponding bromine additions the influence of water is very much greater, 10% of water increasing the rate 100-fold. In the bromine additions it was shown that there was a change from a termolecular to a bimolecular rate. With iodine, no such effect is observable.

This investigation is being extended to the corresponding reactions of chlorine, bromine chloride, and iodine chloride.

VICTORIA UNIVERSITY COLLEGE, WELLINGTON, N.Z. [*Received, December 30th*, 1937.]

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# 32. *Experiments on the Synthesis of Substances related to the Sterols. Part XIX.*

By ROBERT ROBINSON and JAMES WALKER.

The preparation of 1-keto-7-methoxy-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrene-b * has been improved and its conversion into the 2-carbethoxyl derivative is here described in greater detail. The *C*-methylated ester has been subjected to the Reformatsky reaction with ethyl bromoacetate, but no crystalline product could be isolated, doubtless because a complex mixture of substances and stereoisomerides was obtained. An amorphous methylimide of the anticipated composition was separated after treatment with acetic anhydride, hydrolysis, reduction with hydriodic acid and phosphorus, methylation, and heating with methylamine. 1-Keto-7-methoxy-2-methyl-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrene-b was isolated as a by-product from the Reformatsky reaction after hydrolysis and is, of course, obtained from unchanged keto-ester.

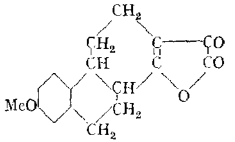
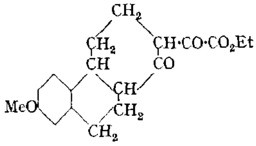
Further work has shown that the Friedel–Crafts reaction applied to certain methoxydihydronaphthalene derivatives (or ketones which can yield these substances by ring closure and dehydration) involves, first, disproportionation with formation of related naphthalene and tetrahydronaphthalene derivatives, and second, acylation in the benzenoid nucleus or naphthalene nucleus in the *o*-position to methoxyl. The acyl group is removed by hydrolysis from the naphthalene derivatives by the action of hydriodic acid, which reagent has also been found to effect ring closure of a methoxynaphthylbutyric acid to a hydroxyketotetrahydrophenanthrene.

ON hydrogenation of 1-keto-7-methoxy-1 : 2 : 3 : 4 : 9 : 10-hexahydrophenanthrene (Robinson and Schlittler, J., 1935, 1288) in ethyl acetate solution (the reaction being incomplete and being carried further in methyl-alcoholic solution) in presence of palladised strontium carbonate, a little more than one-third of the product could be isolated by way of the semicarbazone as dihydro-ketone, the remainder being converted into 7-methoxy-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthr-1-ol. The losses involved in the oxidation of this secondary alcohol to the related ketone by means of chromic acid (J., 1936, 750) or copper oxide (J., 1937, 63) are diminished by the application to this case of the reversed Pondorff method of Oppenauer (*Rec. trav. chim.*, 1937, 56, 137).

The condensation of methoxyoctahydrophenanthrone with ethyl oxalate was repeated as previously described, anhydrous sodium ethoxide in ethereal suspension being used (J., 1936, 751), but, on heating the product for the elimination of carbon monoxide, considerable decomposition ensued. Closer examination has shown that, although our first experience proved that the reaction may proceed normally, a large proportion of a new substance is apt to be produced and this compound decomposes on heating. It is obtained from the normal product by loss of alcohol and is evidently the enolic *lactone* (I). This substance gives a ferric reaction which may be due to hydrolysis or to an enolic

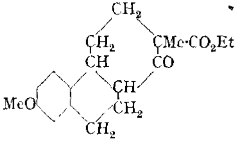
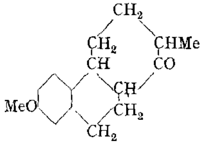
* Reasons have already been given (J., 1936, 748) for the belief that the series-b dealt with in this communication is characterised by *trans*-fusion of the two reduced benzene nuclei.

modification containing the group ⁚C=Ċ—Ċ⁚C(OH)·. The formation of this lactone is avoided by carrying out the condensation in benzene solution and in this way the pure

(I.)   (II.)

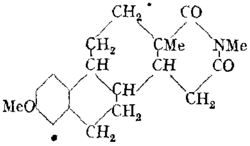
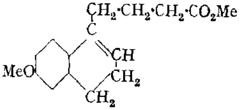
ethoxalyl derivative (II or a related enol) may be isolated. The methylated keto-ester (III) was then obtained as already described and this underwent a rather vigorous reaction when it was treated in hot toluene solution with ethyl bromoacetate and zinc.

Hydrolysis of the product gave a mixture of acids and 1-*keto*-7-*methoxy*-2-*methyl*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene*-b (IV) in proportions indicating that about one third of the keto-ester had undergone the Reformatsky reaction. The acidic

(III.)   (IV.)

product was an intractable mixture and could not be crystallised. After dehydration with hot acetic anhydride the product absorbed only a few c.c. of hydrogen in the presence of a catalyst and it reduced only a trace of alkaline permanganate, the catalytic hydrogenation making very little difference in this respect. The indication was, therefore, that disproportionation to naphthalene and tetrahydronaphthalene derivatives had occurred. Obviously each of these can exist in stereoisomeric forms.

Finally the acids were heated with hydriodic acid and phosphorus, recovered, methylated, and heated with aqueous methylamine so that the water distilled and a temperature of 200° was reached. The nitrogenous products were acidic and neutral and the latter, although not distinctly crystalline, could be fractionated by means of ethyl acetate–light petroleum. An intermediate fraction of indefinite m. p. was an almost colourless solid, the analysis of which tallied well with the formula $C_{20}H_{25}O_3N$. This material is therefore regarded as a mixture of stereoisomerides of the formula (V). A further attempt will be made to utilise the keto-ester (III) for the synthesis of oestrone, although we fear that the methyl group may be in the wrong stereochemical relation to the fused alicyclic rings.

(V.)   (VI.)

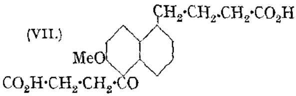
In continuation of experiments reported in Part XVI (Lin, Resuggan, Robinson, and Walker, J., 1937, 68; the work in this case was with the lower homologue of the dihydronaphthalene derivative and γ-carbomethoxybutyryl chloride) we have examined the condensation of the ester (VI) with β-carbomethoxypropionyl chloride in the presence of aluminium chloride. After hydrolysis of the product we were able to separate two *keto-acids*, $C_{19}H_{20}O_6$ and $C_{19}H_{24}O_6$. Both were saturated to permanganate and were

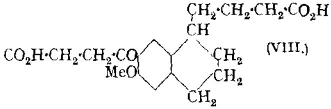
clearly the result of disproportionation of the dihydronaphthalene nucleus with formation of naphthalene and tetrahydronaphthalene derivatives, followed by normal condensations. The attack of the ethenoid double bond, which we had hoped for, evidently does not take place and this conclusion applies also to the condensations described in Part XVI. The constitutions of the isomeric acids therein described are now regarded as analogous to (VII) and (VIII) below.

The products obtained on heating the new acid, $C_{19}H_{20}O_6$, with concentrated hydriodic acid were methyl iodide, succinic acid, and 7-hydroxy-1-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene (Butenandt and Schramm, *Ber.*, 1935, **68**, 2090). A little $\gamma$-6-methoxy-1-naphthylbutyric acid was prepared by oxidation of the dihydro-acid (corresponding to VI) with alkaline permanganate, and when heated with hydriodic acid this also furnished the same hydroxyketotetrahydrophenanthrene. This novel method of ring closure gives an almost quantitative yield in the present instance and it may have considerable preparative value in other cases.

Of more significance in connection with the constitution of the acid $C_{19}H_{20}O_6$ is the removal of the succinyl residue by hydrolysis. The reaction would probably not occur if the chain were attached to the 2-, 4-, or 7-position in the naphthalene nucleus, whereas it would be anticipated if the acid were a 1-acyl-2-naphthol derivative (position 5 in the case under consideration). Specimens of 1-acetyl-2-naphthol and 3-acetyl-2-naphthol were kindly supplied by Dr. W. Baker and it was found that the former was readily hydrolysed by boiling concentrated hydriodic acid with formation of β-naphthol, whereas the latter was unchanged under the same conditions. Therefore we attribute the constitution (VII)

(VII.)




(VIII.)

to the acid $C_{19}H_{20}O_6$. Attempts to equate the acids $C_{19}H_{20}O_6$ and $C_{19}H_{24}O_6$ by dehydrogenating the latter were unsuccessful, but it seems very probable that $C_{19}H_{24}O_6$ is either the tetrahydro-derivative of (VII) or has the structure (VIII).

## Experimental.

1-*Keto-7-methoxy-*1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene.*—(A) 1-Keto-7-methoxy-1 : 2 : 3 : 4 : 9 : 10-hexahydrophenanthrene (22 g.) was hydrogenated in ethyl acetate solution (180 c.c.) under 3 atms. with a palladised strontium carbonate catalyst (16 g. of 2%) for 16 hours; the product then isolated still contained some unreduced material as shown by the colour of the precipitate obtained with Brady's reagent. Hydrogenation was completed in methyl-alcoholic solution and the product was isolated and treated in the manner described previously (J., 1936, 750), yielding the semicarbazone (9·3 g.) of the desired ketone along with methoxyoctahydrophenanthrol (13·5 g.).

(B) 7-Methoxy-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthr-1-ol (18·6 g.), dissolved in acetone (400 c.c.), was added to a solution of aluminium *tert.*-butoxide (33 g.) in dry benzene (800 c.c.) and the mixture was refluxed for 36 hours and worked up as described by Oppenauer (*loc. cit.*). The crude product had the odour of mesityl oxide and this was removed by steam-distillation; further treatment, as above, yielded the semicarbazone (9·7 g.) of the desired ketone along with unchanged secondary alcohol (7·1 g.).

The yield of ketone was not diminished when the aluminium *tert.*-butoxide was replaced by a mixture of aluminium *iso*propoxide and an equivalent amount of *tert.*-butyl alcohol. In one experiment aluminium *iso*propoxide was used without any addition of *tert.*-butyl alcohol and the yield of ketone was diminished, but, as the phenanthrol used in this experiment had been recovered from several previous ones, a more difficultly oxidisable stereoisomeride may have accumulated in it.

As described previously (*loc. cit.*), the hydrolysis of the semicarbazone yielded a mixture of a labile (oil) and a stable (solid) ketone; the latter was freed from the former by crystallisation from methyl alcohol and had the recorded properties.

*Enolic Lactone of* 1-*Keto*-7-*methoxy*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydro*-2-*phenanthroylformic Acid* (I).—1-Keto-7-methoxy-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrene (3·76 g.) and ethyl oxalate (2·5 g.) were dissolved in pure ether (120 c.c.) and freshly prepared alcohol-free sodium ethoxide (1·5 g.) was added in lumps and then disintegrated; an orange sodium derivative soon separated. After 2 days, ether and dilute sulphuric acid were added; the cream-coloured solid then precipitated was collected and dried (0·21 g., m. p. 180—183° with decomp.). The ethereal solution was separated, dried, and evaporated; the resulting orange semi-solid material deposited a further quantity (1·2 g.) of the foregoing solid on crystallisation from alcohol. The alcoholic mother-liquors yielded a mixture (2·7 g.), which was distributed between ether and dilute sodium hydroxide solution. From the ethereal layer a further quantity of the enolic lactone (0·8 g.) was obtained. The alkaline solution afforded the ethyl ester (1·7 g.) described below on acidification and extraction with ether.

The enolic *lactone* (I) separated from alcohol in small cream-coloured prisms, m. p. 184—186° (decomp.) after softening from 180° (Found: C, 71·3; H, 5·7. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·7%). With alcoholic ferric chloride a transient green colour was developed and passed into brown, which became redder on keeping.

*Ethyl* 1-*Keto*-7-*methoxy*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydro*-2-*phenanthroylformate* (II).—1-Keto-7-methoxy-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrene (14·38 g.) and ethyl oxalate (10 g.) were dissolved in dry benzene (120 c.c.) and treated with alcohol-free sodium ethoxide (4·5 g.) in the usual way. After standing for 18 hours in the ice-chest, the clear orange solution was mixed with ether and ice-water and the alkaline layer was rapidly separated and washed with ether. The oil liberated on acidification was taken up in ether, and the extract dried and evaporated. The resulting stiff orange-yellow syrup (18·16 g.) deposited a few crystals and thus allowed recrystallisation to be effected by inoculation. The *compound* separated from ether in long colourless felted needles, m. p. 98—99° with evolution of gas (carbon monoxide) above *ca.* 138° (Found: C, 69·1; H, 6·6. $C_{19}H_{22}O_5$ requires C, 69·1; H, 6·7%). With alcoholic ferric chloride a blood-red colour was developed. The complete lack of colour in this compound contrasts with the orange colour of the analogous compound from ketomethoxyhexahydrophenanthrene in which there is a double bond in the 11 : 12-position (J., 1937, 62); the effect of conjugation through this bond with the aromatic nucleus is noteworthy.

*Ethyl* 1-*Keto*-7-*methoxy*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene*-2-*carboxylate*.—The above αγ-diketo-ester (21 g.) was heated in three equal portions at 170° until the evolution of gas ceased (2—3 hours) and the resulting keto-ester was distilled in small portions (2—3 g. each) at 0·5 mm. (b. p. *ca.* 205°) as a pale yellow, viscous syrup (12·4 g.) giving a pure violet colour with alcoholic ferric chloride.

*Ethyl* 1-*Keto*-7-*methoxy*-2-*methyl*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene*-2-*carboxylate* (III).—Methylation of the preceding β-keto-ester was effected in the manner previously described (*loc. cit.*) with molecular potassium (1·7 g., slight excess) and a large excess of methyl iodide in benzene solution (100 c.c.). The crude product (12·82 g.) distilled as a pale yellow syrup (11·66 g.) at 200—205°/0·45 mm., $n_D^{19.5°}$ 1·5462; it gave no ferric reaction and the observed constants were in good agreement with those already recorded.

*Reformatsky Reaction.* 1-*Keto*-7-*methoxy*-2-*methyl*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene* (IV).—(A) The preceding methylated keto-ester (3·06 g.), ethyl bromoacetate (3·2 c.c.; 3 mols.), pure toluene (15 c.c.), and zinc needles (1·9 g.; 3 at.) were mixed and cautiously warmed after the addition of a crystal of iodine. A brisk reaction set in and after the spontaneous ebullition had moderated the mixture was refluxed (bath 150°) for 1 hour after the addition of more toluene (5 c.c.); a brown viscous complex then separated. Ether and dilute sulphuric acid were added to the cooled mixture and the upper layer was thoroughly washed with dilute sulphuric acid and with water. After several washings with dilute sodium carbonate solution the extract was dried and evaporated, and the crude neutral product (3·36 g.) refluxed for 7 hours with ethyl-alcoholic potassium hydroxide (7 g. of potassium hydroxide in 5 c.c. of water and 15 c.c. of alcohol). The hydrolysis product was separated into an acidic (1·05 g.) and a neutral (1·85 g.) portion in the usual way. The acidic material was a viscous reddish-brown syrup, which showed no tendency to crystallise and was quantitatively esterified by means of an excess of diazomethane (from 5 g. of nitrosomethylurea). The neutral portion was a light brown syrup which crystallised on standing. The *substance* was readily soluble in the usual solvents and recrystallisation from ether afforded fine colourless prisms, m. p. 119—120° (Found: C, 78·6; H, 8·3. $C_{16}H_{20}O_2$ requires C, 78·7; H, 8·2%).

(B) The methyl keto-ester (11·66 g.), ethyl bromoacetate (20·5 c.c.; 5 mols.), and zinc needles (12·5 g.; 5 at.) were allowed to interact as before in pure toluene (40 c.c.) and the mixture was heated for 3 hours under reflux (bath 150°) after the spontaneous reaction had moderated. The ether–toluene solution of the product was well washed with dilute sulphuric acid and then with dilute sodium carbonate solution. From the latter washings there was obtained on acidification and extraction with ether a reddish-brown gum (2·52 g.) giving a brown colour with alcoholic ferric chloride. The neutral material isolated from the ether–toluene solution after drying was a reddish-brown syrup (14·15 g.) and it was immediately hydrolysed under reflux with alcoholic potassium hydroxide (30 g. of potassium hydroxide in 20 c.c. of water and 60 c.c. of alcohol) for 5 hours. An acidic (4·2 g.) and a neutral (6·07 g.) portion were separated as before in the normal way.

The amount of ketone isolated corresponds to 7·86 g. of methyl keto-ester, indicating that 3·80 g. (or 32·6%) of the latter have undergone the Reformatsky reaction.

Neither the ester obtained in (A) nor the acids from (B) could be induced to crystallise. The acids were refluxed with pure acetic anhydride for 30 minutes and isolated as a thick, pale brown syrup, found to be almost saturated towards potassium permanganate. On attempted catalytic reduction the volume of hydrogen absorbed was negligible. Efforts to fractionate the substance with the aid of solvents (readily soluble in chloroform and ethyl acetate; sparingly soluble in alcohol and especially in light petroleum) gave no crystalline material and as a final resource the whole material was collected and refluxed with hydriodic acid (*d* 1·7) and phosphorus, both in large excess. The isolated phenolic acids were uncrystallisable and after methylation in the usual manner the recovered methoxy-acids showed the same behaviour with solvents as the original material. An excess of aqueous methylamine was added, and the solution distilled from a gradually heated oil-bath until the temperature of the bath reached 200°. The brown residue could be separated into an acidic portion (qualitative test for nitrogen, positive), which could not be crystallised, and a neutral portion. The latter was dissolved in ethyl acetate, and a large volume of light petroleum added. The gummy precipitate (after keeping for some hours in the ice-chest) was again dissolved in ethyl acetate, and light petroleum added until turbidity occurred. The solution was kept in the ice-chest, then filtered, and an excess of light petroleum added. On keeping in the ice-chest the chalky precipitate was then obtained as an amorphous solid and repetition of the process gave a pale brownish powder which softened at 130—140° and melted up to about 170° (Found: C, 73·6; H, 7·8; N, 4·1. $C_{20}H_{25}O_3N$ requires C, 73·4; H, 7·6; N, 4·3%. $C_{20}H_{23}O_3N$ requires C, 73·8; H, 7·1; N, 4·3%). The substance was insoluble in aqueous sodium hydroxide, but on boiling it passed into solution. Methylamine was not evolved until the liquid was concentrated by distillation of most of the water.

1-*Keto-7-methoxy-2-hydroxymethylene*-1 : 2 : 3 : 4 : 9 : 10-*hexahydrophenanthrene*.—To a solution of 1-keto-7-methoxy-1 : 2 : 3 : 4 : 9 : 10-hexahydrophenanthrene (10 g.) and amyl formate (6·1 g., freshly distilled) in anhydrous ether (120 c.c.), sodium ethoxide (3·8 g., alcohol-free) was added in lumps and then disintegrated. A buff-coloured sodium derivative rapidly separated and after 14 hours at the room temperature, ice-water was added and the alkaline layer was rapidly separated, washed with ether, and acidified. The precipitated oil, which partly crystallised at once, was taken up in ether, and the extract dried and evaporated, yielding an orange crystalline solid (8 g.). Recrystallisation from aqueous acetic acid (*ca.* 65%) afforded deep yellow plates, m. p. 90—91° (Found: C, 74·7; H, 6·3. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·2%).

1-*Keto-7-methoxy-2-hydroxymethylene*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene* was prepared in a like manner from 1-keto-7-methoxy-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrene (1·1 g.), ethyl formate (0·74 g.), and alcohol-free sodium ethoxide (0·8 g.) in anhydrous ether (40 c.c.). The aqueous alkaline solution on acidification furnished a light orange, crystalline precipitate (1·1 g., m. p. 133°), which was collected, washed, and dried. Recrystallisation from 60% aqueous acetic acid afforded light amber needles, m. p. 140—141° (Found: C, 74·6; H, 7·0. $C_{16}H_{18}O_3$ requires C, 74·4; H, 7·0%).

Neither of the above two compounds underwent smoothly the ring-fission described by Lapworth (J., 1900, 77, 1059) for hydroxymethylenecamphor (cf. Bardhan, J., 1936, 1851). With the former compound a black tar was produced and the only identifiable product was hydrogen cyanide, and with the latter compound, although there was no formation of tar, a satisfactory product was not isolable.

*Condensation of Methyl γ-(6-Methoxy-3 : 4-dihydro-1-naphthyl)butyrate* (VI) *with β-Carbomethoxypropionyl Chloride in the Presence of Aluminium Chloride.*—A mixture of methyl

methoxydihydronaphthylbutyrate (6 g.), carbomethoxypropionyl chloride (6·8 g.), and carbon disulphide (25 c.c.) was rapidly added to a mechanically stirred mixture of powdered aluminium chloride (12·3 g.) and carbon disulphide (75 c.c.) cooled in melting ice. After 3 hours' stirring, the mixture was kept for 12 hours; the carbon disulphide was then decanted, and ice added in order to decompose the complex. Steam was passed for 5 minutes, and the product (10 g.) isolated by means of ether. The product was hydrolysed with aqueous alcoholic potassium hydroxide, remethylated with methyl sulphate and potassium hydroxide, and again hydrolysed and isolated as mixed acids (6 g.), which partly crystallised. The paste was triturated with acetone, and the solid collected and thrice crystallised from acetone; it formed colourless rod-like needles, m. p. 163—164° (Found: C, 65·9, 65·6; H, 6·9, 7·1; MeO, 8·4. $C_{19}H_{24}O_6$ requires C, 65·5; H, 6·9; 1MeO, 8·9%). The *acid* was very sparingly soluble in hot benzene and cold acetone. It was saturated to permanganate, and with 2 : 4-dinitrophenylhydrazine it gave an orange derivative, soluble in aqueous sodium carbonate. Heated with acetic anhydride, it furnished a red insoluble resin. When it was heated with platinum-black or with selenium, extensive decomposition occurred and the corresponding de-tetrahydro-derivative could not be obtained. The first acetone mother-liquor afforded a further quantity of this acid (total yield, 2·3 g.) by treatment with light petroleum and then crystallisation of the insoluble portion from ethyl acetate. The later acetone mother-liquors were concentrated and on keeping in the ice-chest deposited a pale yellow crust of prisms, m. p. 140—147° (1·8 g.). The substance, recrystallised from chloroform, in which it was sparingly soluble, formed colourless prismatic needles, m. p. 155—157° (mixed with $C_{19}H_{24}O_6$, m. p. 140—144°); recrystallisation from ethyl acetate–benzene then gave elongated prisms with pointed ends (Found in material dried at 100°: C, 67·5, 67·5; H, 6·2, 5·9. $C_{19}H_{20}O_6$ with 4·6% $C_6H_6$ requires C, 67·5; H, 5·9%. The presence of benzene was confirmed by Ramsden's test. Found in material dried at 120° in a high vacuum: C, 66·5, 66·6; H, 6·0, 6·0. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8%). This *acid* was saturated to alkaline permanganate and formed an alkali-soluble orange derivative with dinitrophenylhydrazine. In a subsequent experiment the crude mixture of acids (11 g.) was more oily than in the first case and it was accordingly thoroughly extracted with boiling light petroleum (b. p. 60—80°); the magma then hardened. This was dissolved in acetone and seeded with the acid $C_{19}H_{24}O_6$; the filtrate from the crystals of this substance (3·4 g.) was mixed with 2 vols. of benzene and 1 vol. of chloroform; the acid $C_{19}H_{20}O_6$ then separated in a nearly pure form (3·6 g.). It is noteworthy that in the above separation the tetrahydro-acid was the first to crystallise, whereas in the isomeric series previously described the naphthalene acid was much the more sparingly soluble of the two acids obtained. The acid (0·5 g.), m. p. 155—157°, was boiled with hydriodic acid (*d* 1·7, 5 c.c.) in a stream of carbon dioxide for ½ minute; the formation of methyl iodide was recognised by means of alcoholic silver nitrate. The solution was mixed with water and sulphurous acid; a pale yellow precipitate was then obtained (0·3 g.).

The substance crystallised from chloroform in dense clusters of colourless needles, m. p. 232°, and was again crystallised from aqueous acetic acid (Found in material dried at 100°: C, 71·3; H, 5·9. $C_{14}H_{12}O_2,C_2H_4O_2$ requires C, 70·6; H, 5·9%). On methylation, methoxy-tetrahydrophenanthrone was obtained; it was converted into its 2 : 4-dinitrophenylhydrazone, which crystallised from pyridine in red needles, m. p. 304° (decomp.) alone or mixed with a specimen previously examined and analysed (J., 1936, 750). The hydriodic acid aqueous solution was saturated with salt and extracted with ether; succinic acid was thus isolated and recognised as succinanil and by the fluorescein reaction.

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## 33. *Stereochemistry of the Acenaphthylene and Tetrahydro-acenaphthylene Glycols. Part I.*

By KATHLEEN M. JACK and H. GORDON RULE.

Two acenaphthylene glycols are known, of which the lower-melting isomeride has now been proved to have the *trans*-structure by its resolution with the aid of *l*-menthoxyacetyl chloride. The optically active d-*acenaphthylene glycol* exhibited a

dextrorotation when dissolved in non-polar or weakly polar solvents, and a lævorotation in strongly polar media. In liquids of intermediate polarity the rotation approximated to zero.

Reduction of acenaphthenequinone with alcohol and sodium amalgam led to the isolation of trans-1 : 2 : 3 : 4-*tetrahydroacenaphthylene glycol*, which was also formed by the catalytic hydrogenation of *trans*-acenaphthylene glycol dissolved in alcohol at 50°, with platinum-black as catalyst. A corresponding cis-1 : 2 : 3 : 4-*tetrahydroacenaphthylene glycol* has been prepared by catalytic hydrogenation of *cis*-acenaphthylene glycol at 50°. When palladium dispersed on barium sulphate was employed as catalyst, the tendency was for acenaphthene to be formed by elimination of the hydroxyl groups.

A new and greatly improved method of preparing *cis*- and *trans*-acenaphthylene glycols has been found in the catalytic hydrogenation of acenaphthenequinone in cold alcoholic suspension in the presence of platinum-black.

By the interaction of bromine and acenaphthylene and hydrolysis of the resulting mixture of dibromides, Ewan and Cohen (J., 1889, **55**, 578) isolated two acenaphthylene glycols (I), m. p. 159° and 213°. Evidence indicating that the higher-melting form was the *cis*-isomeride was obtained by Criegee, Kraft, and Rank (*Annalen*, 1933, **507**, 194), who condensed it with acetone to give the *iso*propylidene derivative and supported their claim by showing that, like other *cis*-glycols, this form is rapidly oxidised by lead tetra-acetate.

These conclusions have now been verified by the optical resolution of the low-melting glycol, which must therefore be of the *trans*-structure. Resolution was accomplished by use of *l*-menthoxyacetyl chloride, a valuable reagent introduced by Read and Grubb (*J. Soc. Chem. Ind.*, 1932, **51**, 329T). The highly lævorotatory product obtained by fractionation of the mixed *l*-menthoxyacetic esters gave on hydrolysis the active d-trans-*acenaphthylene glycol*, m. p. 158—158·5°. The optical rotation of this compound varied in sign according to the electrochemical nature of the solvent in which it was dissolved (compare Rule and McLean, J., 1931, 674), being dextrorotatory in non-polar media, practically inactive in moderately polar solvents, and lævorotatory in those of strongly polar character. Although the glycol molecules are presumably associated to some extent in benzene solution, even at the low concentrations employed, the effect of this upon the rotatory power is probably small in comparison with the optical change arising from the high degree of solvation of the glycol when dissolved in strongly polar solvents such as acetone or nitrobenzene. For this reason the benzene solutions may be considered the more normal and in the absence of other evidence the enantiomorph under examination is described as the *d*-form. Owing to the very low solubility of the glycol in the majority of organic liquids it was not found possible to make an extended examination of its optical properties; the dispersion in acetone solution, however, was found to be normal. As is not unexpected considering the polar nature of the glycol, the rotatory power in solution is so dominated by the polarity of the solvent that no visible relationship to the refractive index of the medium can be traced. The optical behaviour in solution thus resembles that of *l*-benzoin methyl ether (Rule and Crawford, J., 1937, 140) and is in complete contrast to that of the non-polar saturated hydrocarbon *d*-pinane (Rule and Chambers, J., 1937, 145), the rotatory power of which depends mainly upon the refractive properties of the solution.

*Specific Rotatory Powers of* trans-*Acenaphthylene Glycol in Solution* (l = 4; t = 20°).

| Solvent. | *c*. | α (obs.). | $[\alpha]_{5461}$. | μ. | Solvent. | *c*. | α (obs.). | $[\alpha]_{5461}$. | μ. |
|---|---|---|---|---|---|---|---|---|---|
| Benzene ......... | 0·080 | +0·21° | +66° | 0 | Methyl alcohol | 0·378 | ±0° | 0° | 1·64 |
| Chloroform ...... | 0·392 | +0·81 | +52 | 1·18 | Acetone ......... | 0·400 | −0·39 * | −25 | 2·76 |
| Ethyl alcohol ... | 0·372 | ±0 | 0 | 1·63 | Nitrobenzene ... | 0·324 | −0·49 * | −76 | 3·98 |

* *l* = 2. The polarity of the solvent is indicated by the value of its dipole moment, μ.

Preparation of the acenaphthylene glycols by way of the corresponding bromides is a tedious process which only leads to small yields, chiefly on account of the difficulty in obtaining the starting material acenaphthylene. An alternative method of preparing

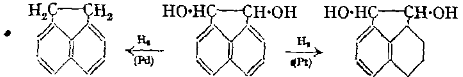
*cis*-acenaphthylene glycol due to Blount and Weissberger (J., 1936, 336), in which acenaphthenequinone is reduced with alcohol and sodium amalgam in an atmosphere of nitrogen, gave in our hands only a compound, m. p. 208·5—209°, later found to be a trans-*tetrahydroacenaphthylene glycol* (II); despite variations in time of reduction, temperature, and proportion of amalgam, none of the *cis*-acenaphthylene glycol could be obtained. The new tetrahydro-glycol gave a diacetate and did not react with bromine at the ordinary temperature. All four additional hydrogen atoms must therefore have entered the same ring in the acenaphthylene nucleus.

A tetrahydroacenaphthylene glycol of this type contains three asymmetric carbon atoms and should be capable of existing in eight stereoisomeric forms, comprising four racemic modifications. The form obtained by chemical reduction of the quinone could not be condensed with acetone, but even apart from the uncertainty which attaches to negative evidence, this is insufficient to characterise the compound as possessing a *trans*-configuration, since it has been concluded by Böeseken (*Rec. trav. chim.*, 1921, **40**, 566) that the formation of such condensation products occurs only when the hydroxyl groups are in the same plane as the carbon atoms to which they are linked and lie on the same side of them. Although these conditions are fulfilled in the case of *cis*-acenaphthylene glycol, they do not hold in that of its tetrahydro-derivative, as an inspection of the space model makes clear.

An unequivocal method of establishing the structure of the tetrahydro-glycol would be to prepare it from either the *cis*- or the *trans*-acenaphthylene glycol. Experiment showed that it could be obtained in excellent yield from the *trans*-glycol by catalytic hydrogenation, thus proving it to have a *trans*-arrangement of the hydroxyl groups. On the other hand, the hydrogenation of *cis*-acenaphthylene glycol under the same conditions led to the isolation of a cis-*tetrahydroacenaphthylene glycol*, m. p. 92·5—93·5°, in which all four hydrogen atoms had also entered the same ring in the nucleus. It is of interest that this *cis*-compound readily yields an *acetone* derivative even though one of the hydroxyl groups must be displaced in some degree from the plane occupied by the remaining hydroxyl group and the two carbon atoms of the acenaphthylene bridge.

Among the acenaphthylene glycols the higher-melting, less soluble isomeride (m. p. 213°) is the *cis*-form, whereas among the tetrahydroacenaphthylene glycols now isolated it is the *trans*-form (m. p. 209°). In view of the statement of Blount and Weissberger (*loc. cit.*) that they prepared *cis*-acenaphthylene glycol by reducing acenaphthenequinone with sodium amalgam, efforts were made during the present work to repeat this result by employing less vigorous conditions than those which had been found to lead to a tetrahydro-compound. In every case, however, *trans*-tetrahydroacenaphthylene glycol alone could be isolated in a state of purity. The two glycols in question have approximately the same melting points and are thus liable to be confused with one another, but each compound is also very much less soluble than its corresponding geometrical isomeride and it should therefore be possible to isolate either product at will by controlling the amount of hydrogen taken up.

Variation in the catalyst employed in the above hydrogenations led to an interesting difference in the product. Thus the use of palladium dispersed on barium sulphate caused reduction of the hydroxyl groups and formation of acenaphthene (III) in high yield. A small amount of acenaphthene was also obtained by the hydrogenation of the *cis*-glycol in the presence of platinum catalyst. The main reactions thus appear to proceed as indicated in the following scheme:




(III.) (I.) (II.)

A greatly improved method of preparing *cis*- and *trans*-acenaphthylene glycols is the catalytic hydrogenation of acenaphthenequinone suspended in cold alcohol in the presence of platinum catalyst. The resulting mixture of glycols is readily separated by crystallis-

ation from water and the compounds may thus be prepared in a few hours and in good yields.

## Experimental.

Acenaphthylene was prepared by passing the vapour of acenaphthene through a red-hot silica tube in an atmosphere of carbon dioxide (Dziewonski and Rapalski, *Ber.*, 1912, **45**, 2491), the maximum yield (47%) being obtained when the tube was packed with porous tile. Separation from unchanged acenaphthene was effected by recrystallisation of the mixed picrates.

Acenaphthylene dibromides (Blumenthal, *Ber.*, 1874, **7**, 1093) were prepared by slow addition of bromine to an ethereal solution of the hydrocarbon at − 10°. As both the *cis*- and the *trans*-glycol were desired, the mixture of dibromides obtained by evaporation of the ether and hydrogen bromide was hydrolysed directly by boiling for 1 hour with water (Graebe and Jequier, *Annalen*, 1896, **290**, 205). The less soluble *cis*-acenaphthylene glycol was deposited on cooling, and after recrystallisation (charcoal) was obtained in long silky needles, m. p. 212—213° (Graebe and Jequier and Ewan and Cohen record m. p. 204°; Criegee, Kraft, and Rank found 209—210°). The *trans*-glycol remained on evaporation of the mother-liquors from the *cis*-compound, the crude product melting at about 145°. In purifying this isomeride various methods were applied, including oxidation of the small content (about 18%) of *cis*-glycol present by use of lead tetra-acetate, as recommended by Criegee, Kraft, and Rank. The most convenient procedure was found in treating the crude *trans*-glycol, suspended in dry acetone, with 1% of hydrogen chloride and some anhydrous sodium sulphate. After 24 hours at room temperature any undissolved *trans*-glycol was brought into solution by further addition of acetone, and dry ammonia passed in to neutralise hydrogen chloride. The filtered solution was evaporated, and the acetone derivative of the *cis*-glycol boiled out with light petroleum, in which *trans*-acenaphthylene glycol is very sparingly soluble. Crystallisation of the latter from water gave the pure glycol, m. p. 159·5°. In a typical preparation 8 g. of acenaphthylene gave 1·7 g. of *cis*-glycol, m. p. 207—208°, and 0·88 g. of *trans*-glycol, m. p. 157°, the total yield of 2·58 g. representing 26% of the theoretical. In the literature no yields are recorded for these preparations.

*Resolution of* trans-*Acenaphthylene Glycol*.—The racemic glycol (2 g.) in pyridine (20 c.c.) was esterified with *l*-menthoxyacetyl chloride (7 g.). The resulting sticky solid was recrystallised four times from light petroleum, giving colourless needles (1·03 g.) of d-trans-*acenaphthylene glycol di*-l-*menthoxyacetate*, m. p. 114—115°; $[\alpha]_{5461}^{20°}$ − 327·3° in benzene ($c$ = 0·414), the rotatory power being unaltered by continued recrystallisation (Found: C, 74·6; H, 8·7. $C_{36}H_{50}O_6$ requires C, 74·7; H, 8·7%).

The diester on hydrolysis with hot aqueous alcoholic sodium hydroxide gave a quantitative yield of d-trans-*acenaphthylene glycol*, which separated from water in colourless needles, m. p. 158—158·5° (depressed to 149—152° by the inactive glycol). Rotatory powers are given on p. 189 (Found: C, 77·4; H, 5·45. $C_{12}H_{10}O_2$ requires C, 77·2; H, 5·6%). An attempt to isolate the remaining optical isomeride from the mother-liquors obtained from the above ester was unsuccessful.

In a similar manner *cis*-acenaphthylene glycol was treated with *l*-menthoxyacetyl chloride and pyridine. The crude product, after being crystallised four times from light petroleum, afforded cis-*acenaphthylene glycol di*-l-*menthoxyacetate*, m. p. 40—42°; $[\alpha]_{5461}^{20°}$ − 114·8° in benzene ($c$ = 0·418), these values being unchanged by further crystallisation (Found: C, 74·8; H, 8·9%). On hydrolysis with alcoholic potassium hydroxide the ester gave a quantitative yield of inactive *cis*-glycol (checked by mixed m. p.).

*Reduction of Acenaphthenequinone with* (2½%) *Sodium Amalgam*.—Reduction was effected in alcoholic solution with stirring at 50° and in an atmosphere of nitrogen as described by Blount and Weissberger (*loc. cit.*). At first a considerable deposition of dark blue solid occurred, later the tint changed to blue green and most of the solid passed into solution. After treatment with acetic acid and removal of mercury, the addition of water precipitated a yellow solid containing unchanged quinone (checked by mixed m. p.). The filtrate on evaporation gave a solid, m. p. 202—203° (38% of the theoretical yield) which on recrystallisation did not give the expected colourless needles of *cis*-acenaphthylene glycol, but plates, m. p. 208·5—209°, later proved to consist of trans-1 : 2 : 3 : 4-*tetrahydroacenaphthylene glycol* (the mixed m. p. with *cis*-acenaphthylene glycol, m. p. 212°, was strongly depressed) (Found: C, 75·5; H, 7·3. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%).

This compound, when heated with acetic anhydride, was converted quantitatively into

trans-*tetrahydroacenaphthylene glycol diacetate*, which crystallised in colourless plates, m. p. 139—140°, from aqueous alcohol (Found: C, 70·1; H, 6·5; *M*, by Rast method, 249. $C_{16}H_{18}O_4$ requires C, 70·1; H, 6·6%; *M*, 274). The glycol gave no condensation product with acetone, nor did it decolourise bromine in warm chloroform solution.

The above preparation was also carried out at 65—70°, an additional 33% of sodium amalgam being used; the time of reduction was varied in different preparations from 12 to 33 hours. The highest yield of pure tetrahydro-glycol was 32%, obtained by stirring the reactants for 24 hours at 65—70° and using 400 g. of amalgam to 5·5 g. of quinone.

By treatment with *l*-menthoxyacetyl chloride and pyridine the above glycol was converted into trans-*tetrahydroacenaphthylene glycol di-l-menthoxyacetate*, which crystallised from aqueous alcohol in colourless needles, m. p. 71—72°, $[\alpha]^{20°}_{5461}$ − 96° in benzene (*c* = 0·520) (Found: C, 73·9; H, 9·1. $C_{36}H_{54}O_6$ requires C, 74·2; H, 9·3%). The rotatory power of the ester was unchanged on repeated crystallisation, and on hydrolysis the original glycol was regenerated (confirmed by mixed m. p.), which was inactive in non-polar as well as in polar solvents.

*Catalytic Hydrogenation of* trans-*Acenaphthylene Glycol*.—Hydrogenation was carried out at 3 atms. and 50°, the glycol (1·86 g.) being dissolved in alcohol (50 c.c.), in the presence of 0·1 g. of platinum catalyst (prepared according to Adams, Voorhees, and Shriner, *Organic Syntheses*, 1928, **8**, 92). A few drops of concentrated hydrochloric acid and of aqueous ferric chloride were added as accelerators. After absorption of the required amount of gas the filtered liquid was diluted with water, affording crystalline plates of *trans*-tetrahydroacenaphthylene glycol, m. p. 208° alone or admixed with the product obtained by chemical reduction of acenaphthenequinone. A further quantity was recovered from the aqueous alcoholic mother-liquors, the total yield being 75% of the theoretical.

*Catalytic Hydrogenation of* cis-*Acenaphthylene Glycol*.—The same quantities and conditions as given above for the *trans*-compound being used, a solid (1·78 g.) was obtained, part of which was insoluble in water and consisted of acenaphthene, m. p. 92° (confirmed by mixed m. p.). The water-soluble fraction on purification proved to be cis-1 : 2 : 3 : 4-*tetrahydroacenaphthylene glycol* (0·5 g.), which separated from light petroleum in needles, m. p. 92·5—93·5° (Found: C, 75·4; H, 7·0. $C_{12}H_{14}O_2$ requires C, 75·7, H, 7·3%). In warm chloroform solution the compound did not decolourise bromine.

When the glycol (0·66 g.) was kept for 12 hours in dry acetone with addition of a little concentrated sulphuric acid, it afforded the *isopropylidene* derivative (0·7 g., m. p. 49—50°), which crystallised from light petroleum in needles, m. p. 51—52° (Found: C, 78·5; H, 7·7. $C_{15}H_{18}O_2$ requires C, 78·3; H, 7·8%).

Treatment with acetic anhydride converted the glycol quantitatively into cis-1 : 2 : 3 : 4-*tetrahydroacenaphthylene glycol diacetate*, which crystallised from light petroleum in needles, m. p. 121—121·5° (Found: C, 70·0; H, 6·3. $C_{16}H_{18}O_4$ requires C, 70·0; H, 6·6%).

When hydrogenation was carried out at 50° with *cis*-acenaphthylene glycol (1·9 g.), alcohol (50 c.c.), and a palladium catalyst (0·5 g., prepared by reducing 1·7 g. of palladium chloride with formalin in a suspension of 20 g. of freshly precipitated barium sulphate), the only product isolated was acenaphthene (1·5 g.).

*Catalytic Hydrogenation of Acenaphthenequinone*.—The quinone (19 g.), suspended in cold alcohol (200 c.c.), was hydrogenated with vigorous shaking in the presence of platinum catalyst (1 g.) for about 12 hours. After the required amount of hydrogen had been absorbed, the precipitated solid was filtered off and recrystallised from alcohol, affording colourless needles of *cis*-acenaphthylene glycol (7 g.), m. p. 207—208°. The filtrate from the reaction mixture was evaporated to dryness, and the yellowish-brown residue crystallised from water (charcoal), giving the *trans*-acenaphthylene glycol (4·5 g.), m. p. 157°. Both products were identified by mixed melting points.

One of the authors (K. M. J.) desires to thank the Edinburgh Angus Club for the award of a Strathmore-Cobb Scholarship.

University of Edinburgh. [*Received, December 7th*, 1937.]

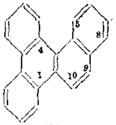
# 34. *Polycyclic Aromatic Hydrocarbons. Part XVI.* 1 : 2 : 3 : 4-*Dibenzphenanthrene.*

By C. L. HEWETT.

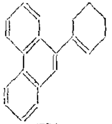
1 : 2 : 3 : 4-*Dibenzphenanthrene* has been synthesised by the Pschorr method from *o*-amino-α-9-phenanthrylcinnamic acid. The cyclisation of 1-(β-9′-*phenanthrylethyl*)-$\Delta^1$-cyclo*hexene* has been carried out, but has been shown to give a *spiran* and not the expected octahydrodibenzphenanthrene. The cyclisation of 1-(β-9′-phenanthrylethyl)-$\Delta^1$-*cyclo*pentene is discussed.

THE three pentacyclic hydrocarbons composed entirely of six-membered aromatic rings which have not yet been described are all derivatives of the feebly carcinogenic hydrocarbon 3 : 4-benzphenanthrene. Furthermore, 2-methyl-3 : 4-benzphenanthrene (Hewett, J., 1936, 596) is a carcinogenic hydrocarbon of considerable potency, as it produces tumours more rapidly than 1 : 2 : 5 : 6-dibenzanthracene, and almost as rapidly as the very active compounds of the cholanthrene and 3 : 4-benzpyrene groups (Bachmann *et al.*, *Proc. Roy. Soc.*, 1937, *B*, 123, 349).

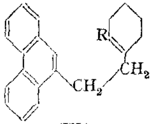
Hence, although most of the existing carcinogenic compounds are related to 1 : 2-benzanthracene, the above considerations suggest that it may be possible to obtain a new group of active compounds, derived from 3 : 4-benzphenanthrene. 1 : 2 : 3 : 4-*Dibenzphenanthrene* (I) has now been synthesised and is being tested for carcinogenic activity. It bears the same relationship to 2-methyl-3 : 4-benzphenanthrene as 1 : 2 : 5 : 6-dibenzanthracene does to the less potent 5-methyl-1 : 2-benzanthracene.



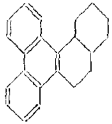

(I.)



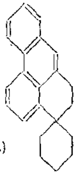
(II.)



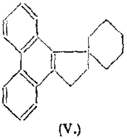

(III.)



(VI.)



(IV.)



(V.)

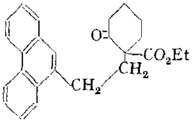
Bergmann and Bergmann (*J. Amer. Chem. Soc.*, 1937, **59**, 1443) attempted to synthesise 1 : 2 : 3 : 4-dibenzphenanthrene by the Diels–Alder diene reaction. They found that 1-9′-phenanthryl-$\Delta^1$-*cyclo*hexene (II) failed to react with maleic anhydride, although the corresponding *cyclo*pentene derivative reacted smoothly.

An attempt to obtain the desired ring system by the cyclisation of 1-(β-9′-*phenanthrylethyl*)-$\Delta^1$-cyclo*hexene* (III; R = H) by means of aluminium chloride has likewise met with no success. Instead of the desired octahydrodibenzphenanthrene (VI), the only product isolated was a *spiran* (probably IV, although V is not excluded), which was obtained in 80% yield. This spiran was recovered unchanged after 24 hours' heating with selenium at 300°, treatment which would be expected to dehydrogenate (VI) but not (IV) or (V) (Cook and Hewett, J., **1933**, 1109; **1934**, 372). Avoidance of spiran formation in analogous cases has been achieved by the introduction of a methyl group, which is subsequently expelled by dehydrogenation, but in view of the unsatisfactory results obtained by Cook, Haslewood, and Robinson in the cyclisation of 2-methyl-1-(β-1′-acenaphthylethyl)-$\Delta^1$-

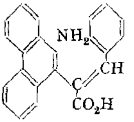
*cyclo*hexene (J., 1935, 670) the cyclisation of the corresponding 2-methyl-*cyclo*hexene (III; R = Me) was not attempted.

Subsequent to these experiments, Bergmann and Blum-Bergmann (*J. Amer. Chem. Soc.*, 1936, **58**, 1678) claimed to have obtained *cyclo*pentenotriphenylene by the cyclisation of 1-(β-9′-phenanthrylethyl)-$\Delta^1$-*cyclo*pentene (analogous to III) by means of aluminium chloride, followed by dehydrogenation. In view of the results now described, it would appear that their compound, m. p. 105·5—107°, regarded by them as tetrahydro*cyclo*pentanotriphenylene, is in fact a spiran and that its dehydrogenation product, alleged to be *cyclo*pentenotriphenylene, is actually a methyl-3 : 4-benzpyrene (compare Cook and Hewett, J., 1934, 372). This would accord with the small yield of product and the resistance to dehydrogenation, for some of the tetrahydro-compound was recovered after 20 hours' heating with selenium at 330—340°. Also the colours of the dehydrogenation product and of its picrate are more in keeping with the benzpyrene structure.

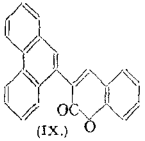
The cyclisation of ethyl 2-(β-9′-phenanthrylethyl)*cyclo*hexanone-2-carboxylate (VII) by boiling 65% sulphuric acid was attempted, but no crystalline products could be isolated.



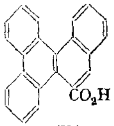
(VII.)



(VIII.)



(IX.)



(X.)

The synthesis of 1 : 2 : 3 : 4-dibenzphenanthrene was eventually accomplished from 9-phenanthrylacetic acid by the Pschorr reaction. An attempted simplification of the preparation of this acid by the oxidation of 9-allylphenanthrene (the preparation of which was published by Bergmann and Blum-Bergmann, *loc. cit.*, while this work was in progress) by means of potassium permanganate in acetone solution (compare the oxidation of 1-allylnaphthalene; Keach, *J. Amer. Chem. Soc.*, 1933, **55**, 2974; Higginbottom and Short, *Rec. trav. chim.*, 1934, **53**, 1141) was impracticable owing to the simultaneous formation of considerable amounts of 9-phenanthroic acid, presumably from the propenylphenanthrene which is known to be formed by migration of the double bond under the influence of alkali (Bergmann and Blum-Bergmann). Hill and Short (J., 1937, 260), however, have shown that arylacetic acids can be obtained in yields of 40% by oxidation of the corresponding allyl compounds by means of potassium permanganate in the presence of acetic acid, only traces of the arylcarboxylic acids being obtained. The procedure of Mosettig and van de Kamp (*J. Amer. Chem. Soc.*, 1933, **55**, 2995) for the preparation of 9-phenanthrylacetic acid was improved by using a simpler route to 9-phenanthraldehyde, which was obtained in excellent yield by hydrolysis of the acetal resulting from interaction of ethyl orthoformate with 9-phenanthrylmagnesium bromide. Miller and Bachmann (*J. Amer. Chem. Soc.*, 1935, **57**, 769) have prepared 9-phenanthraldehyde by this method, but in yields of only 46%.

o-*Nitro-α-9-phenanthrylcinnamic acid* was reduced to the *amino-acid* (VIII) by means of ferrous hydroxide, and decomposition with copper powder at 50° of the sparingly soluble diazonium sulphate obtained from this amino-acid led to a mixture of acids, from which the hydroxy-acid was separated in the form of its *lactone* (IX) by means of methyl-alcoholic hydrogen chloride. 1 : 2 : 3 : 4-*Dibenz*-10-*phenanthroic acid* (X), which was not esterified by this treatment, was then readily isolated. It was decarboxylated to 1 : 2 : 3 : 4-dibenzphenanthrene by copper powder in boiling quinoline. The hydrocarbon, obtained in good yield, was purified through its *picrate*. On oxidation with sodium dichromate it passed into 1 : 2 : 3 : 4-*dibenzphenanthraquinone*, the ortho-quinonoid character of which was shown by its conversion into an *azine* by *o*-phenylenediamine.

## Experimental.

1-(β-9′-*Phenanthrylethyl*)-$\Delta^1$-cyclo*hexene* (III; R = H).—*cyclo*Hexanone (6 g.) was added to an ice-cold Grignard solution prepared from β-9-phenanthrylethyl chloride (Bergmann and

Blum-Bergmann, *J. Amer. Chem. Soc.*, 1936, **58**, 1678) (10·5 g.), magnesium (1·1 g.), ether (35 c.c.), and benzene (15 c.c.). After 2 hours' boiling, the product was decomposed with ice and ammonium chloride, the ethereal solution washed, dried, and evaporated, and the residue distilled. The fraction (10·5 g.), b. p. 220—240°/0·4 mm., was heated with potassium hydrogen sulphate (15 g.) at 160—180° for 1 hour, and the product extracted with ether and distilled, b. p. 200—220°/0·5 mm. (9 g.). The *hydrocarbon* was purified by crystallisation from alcohol of its yellow picrate, m. p. 120—121°, and then formed a viscous oil, b. p. 205—206°/0·4 mm. (Found: C, 91·3; H, 7·9. $C_{22}H_{22}$ requires C, 92·2; H, 7·8%).

*Cyclisation.* A solution of the unsaturated hydrocarbon (5·2 g.) in carbon disulphide (52 c.c.) was treated at 0° with aluminium chloride (5·2 g.) and kept at 2—3° for 5 hours. Ice and hydrochloric acid were then added and the carbon disulphide solution was washed, dried, and evaporated. The residue was distilled over sodium, b. p. 205—210°/0·3 mm., and the solid distillate (4·6 g.) recrystallised from ethyl alcohol. The product, probably *dihydrobenzanthrene-spiro*cyclo*hexane* (IV), formed small colourless plates (3 g.), m. p. 131—132° (Found: C, 92·3; H, 7·8. $C_{22}H_{22}$ requires C, 92·2; H, 7·8%).

β-9-*Phenanthrylethyl Bromide*.—Phosphorus tribromide (50 g.) was slowly added to a solution of β-9-phenanthrylethyl alcohol (Bergmann and Blum-Bergmann, *loc. cit.*) (38 g.) in carbon tetrachloride (100 c.c.) at 60°. After 20 minutes' heating, the solution was cooled, washed with water and dilute sodium carbonate solution, dried, and distilled. The fraction (11 g.), b. p. 200—210°/0·5 mm., was twice recrystallised from ethyl alcohol. β-9-*Phenanthrylethyl bromide* formed colourless needles, m. p. 86—86·5° (Found: C, 67·8; H, 4·8. $C_{16}H_{13}Br$ requires C, 67·4; H, 4·6%).

*Ethyl* 2-(β-9'-*Phenanthrylethyl*)cyclo*hexanone*-2-*carboxylate* (VII).—The potassio-compound prepared from potassium (2·3 g.), ethyl *cyclo*hexanone-2-carboxylate (9·8 g.), and toluene (100 c.c.) was treated with β-9-phenanthrylethyl bromide (11·2 g.) at the b. p. for 60 hours. The whole was then washed with water, the toluene removed, and the residue heated to 240°/0·4 mm. in order to remove low-boiling products and dissolved in ether. The filtered solution was evaporated; the residual keto-ester (13 g.) gave on hydrolysis with potassium hydroxide in aqueous alcohol α-(β-9-*phenanthrylethyl*)*pimelic acid*, m. p. 86—90°, after three crystallisations from benzene (Found: C, 76·1; H, 6·75. $C_{23}H_{24}O_4$ requires C, 75·8; H, 6·65%).

The keto-ester (VII) (8·5 g.) was refluxed with sulphuric acid (100 c.c.) and water (100 c.c.) for 16 hours. The product was extracted with ether and distilled, b. p. 220—230°/0·3 mm. (1·7 g.). After dehydrogenation with selenium (1·5 g.) at 330° for 24 hours, only 0·3 g. of non-crystallisable material was obtained.

*Oxidation of* 9-*Allylphenanthrene*.—A solution of allylphenanthrene (17 g.) in acetone (170 c.c.) was cooled in a freezing mixture, and potassium permanganate (52 g.) slowly added. After some hours the solution was diluted with water and decolourised with sulphur dioxide. The whole was extracted with ether, and the crude acids separated by means of sodium carbonate solution. The mixture of acids was esterified with methyl-alcoholic hydrogen chloride, and the esters distilled, b. p. 174—189°/0·3 mm. (12 g.). This mixture, after solidifying, was crystallised from methyl alcohol, giving long colourless needles (3·5 g.), m. p. 114—115°, of methyl phenanthrene-9-carboxylate (Shoppee, J., 1933, 39, gives m. p. 115°) (Found: C, 81·3; H, 5·1. Calc.: C, 81·6; H, 5·0%). Hydrolysis yielded 9-phenanthroic acid, m. p. 257—258° alone or mixed with an authentic specimen.

The mother-liquors of the ester were distilled, and the fraction, b. p. 175—185°/0·5 mm., collected (7 g.). On hydrolysis with alcoholic potassium hydroxide this gave a mixture of acids (6 g.), from which sodium 9-phenanthrylacetate was obtained by solution in ethyl alcohol (70 c.c.) and addition of sodium hydroxide (1·5 g.) dissolved in a little water. After crystallisation from acetic acid the 9-phenanthrylacetic acid (3 g.) had m. p. 221—222°, not depressed by an authentic specimen but depressed by 9-phenanthroic acid.

9-*Phenanthraldehyde* (compare Miller and Bachmann, *loc. cit.*).—The Grignard solution prepared from 9-bromophenanthrene (104 g.), magnesium (10 g.), anisole (200 c.c.), and ether (180 c.c.) (Shoppee, *loc. cit.*) was cooled in ice and treated with freshly distilled ethyl orthoformate (65·2 g.). The mixture, after being kept in ice for ½ hour and boiled for 2 hours, was decomposed with ice and hydrochloric acid, the volatile matter distilled in steam, the residue boiled for ½ hour, and the solid aldehyde extracted with hot benzene, dried, and distilled, b. p. 180—190°/0·5 mm. (71 g.). After crystallisation from alcohol it had m. p. 99—100° (61 g., a further amount being recovered from the liquor).

o-*Nitro*-α-9-*phenanthrylcinnamic Acid*.—Sodium 9-phenanthrylacetate (62 g., which crystallised when the calculated amount of sodium hydroxide was added to an alcoholic solution of the

acid), acetic anhydride (400 c.c.), and *o*-nitrobenzaldehyde (55 g.) were heated at 125—130° for 7½ hours and poured into 1½ l. of water. After 12 hours, the solution was decanted, and the red resin digested with dilute aqueous ammonia for 2 hours on the water-bath. The solution was boiled (charcoal), filtered, and acidified. The acid was redissolved in 1 l. of N-ammonia and allowed to cool slowly; the ammonium salt, which separated, was collected, dissolved in hot water, and acidified. The liquor of the ammonium salt contained only *o*-nitrocinnamic acid. o-*Nitro-α-(9-phenanthryl)cinnamic acid* (41·5 g.) separated from alcohol in canary-yellow needles, m. p. 214—215° (Found: C, 74·1; H, 4·4. $C_{23}H_{15}O_4N$ requires C, 74·8; H, 4·1%).

o-*Amino-α-(9-phenanthryl)cinnamic Acid* (VIII).—The foregoing nitro-acid (40·5 g.) was heated on the water-bath with ferrous sulphate (400 g.), aqueous ammonia (200 c.c.; *d* 0·880), and water (2 l.) for 2 hours. The ferric hydroxide sludge was extracted ten times with boiling 2% aqueous ammonia, and the combined extracts together with the original filtrate were made just slightly acid with dilute acetic acid. The *amino-acid* was converted by potassium carbonate solution into the potassium salt, which was recrystallised from dilute potassium carbonate solution and decomposed with acetic acid. The free acid (20 g.) separated from benzene as a yellow crystalline powder, m. p. 195—196° (Found: C, 81·7; H, 5·3. $C_{23}H_{17}O_2N$ requires C, 81·4; H, 5·05%).

1 : 2 : 3 : 4-*Dibenz-10-phenanthroic Acid* (X).—The amino-acid (16 g.) was made into a paste with water (50 c.c.), potassium carbonate (8·2 g.), and potassium nitrite (5·5 g.), cooled, and slowly run into 5N-sulphuric acid (400 c.c.) at 0°. Copper powder was added and, when the evolution of nitrogen ceased, the whole was warmed at 50° for 1 hour. A solution of the solid deposit in aqueous sodium carbonate solution was boiled (charcoal), filtered, and acidified and the acids were extracted in ether, dried, recovered, and treated with methyl alcohol and hydrogen chloride. After dilution with water the whole was shaken with ether, the ethereal solution twice extracted with dilute sodium hydroxide solution, and the extract acidified. The acid was purified through the sodium salt and after two crystallisations from acetic acid 1 : 2 : 3 : 4-*dibenz-10-phenanthroic acid* (X) was obtained (3·4 g.), m. p. 266—267°. A portion was sublimed at 260°/0·5 mm.; it then separated from acetic acid in pale yellow needles, m. p. 267—268° (Found: C, 85·3; H, 4·5. $C_{23}H_{14}O_2$ requires C, 85·7; H, 4·4%).

The neutral fraction obtained from the ether on evaporation was triturated with acetone, and the solid thrice crystallised from xylene; it formed colourless plates of *3-(9′-phenanthryl)-coumarin* (IX) (Found: C, 85·8; H, 4·5. $C_{23}H_{14}O_2$ requires C, 85·7; H, 4·4%).

1 : 2 : 3 : 4-*Dibenzphenanthrene* (I).—The acid (X) (3·2 g.) was dissolved in quinoline (30 c.c.) and boiled for 3 hours with copper bronze (1·5 g.). The solution was diluted with ether, filtered from copper, washed with dilute hydrochloric acid and with dilute sodium hydroxide solution, dried, and evaporated. The residue (2·7 g.) was converted into the picrate with picric acid (2·7 g.) in acetic acid solution, the picrate decomposed, and the hydrocarbon distilled from an oil-bath at 270—280°/0·3 mm. After recrystallisation from glacial acetic acid 1 : 2 : 3 : 4-*dibenzphenanthrene* (I) formed colourless needles (1·85 g.), m. p. 114·5—115° (Found: C, 94·85; H, 5·2. $C_{22}H_{14}$ requires C, 94·9; H, 5·1%).

The *picrate* separated in scarlet needles, m. p. 140—140·5°, from acetic acid containing a little picric acid (Found: C, 66·0; H, 3·5. $C_{22}H_{14},C_6H_3O_7N_3$ requires C, 66·25; H, 3·4%).

1 : 2 : 3 : 4-*Dibenzphenanthraquinone*.—The hydrocarbon (0·1 g.) was dissolved in acetic acid (2 c.c.) and boiled with sodium dichromate (0·2 g.) for 5 minutes. Water was added, and the red precipitate filtered off, dried, and recrystallised twice from toluene and once from ethyl acetate; it then formed bright red needles, m. p. 237—238° (Found: C, 85·5; H, 4·1. $C_{22}H_{12}O_2$ requires C, 85·7; H, 3·9%). The *azine* derivative, prepared with *o*-phenylenediamine in acetic acid solution, recrystallised from toluene in canary-yellow needles, m. p. 242—243° (Found: C, 88·2; H, 4·3; N, 7·7. $C_{28}H_{16}N_2$ requires C, 88·4; H, 4·2; N, 7·4%).

The author is indebted to the British Empire Cancer Campaign for a grant to the Hospital which has assisted this work.

Research Institute of the Royal Cancer Hospital (Free),
London, S.W. 3. [*Received, December 16th, 1937.*]

# 35. *The Structure of Germanous Iodide.*

By H. M. Powell and F. M. Brewer.

A modified method of preparing germanous iodide is described. X-Ray investigation shows the crystal structure of the substance to be the C.6 type, and therefore establishes the existence of the germanous ion. The radius of this ion for sodium chloride type structures is estimated to be 0·98 A.

Similarities in the behaviour of germanous and stannous compounds and the close resemblance of germanous iodide to lead iodide (Brewer and Dennis, *J. Physical Chem.*, 1927, **31**, 1526; Brewer, *ibid.*, p. 1817) make it of interest to examine further the evidence for the existence of a germanous ion, and the existence of an " inert pair " of electrons in this element (cf. Sidgwick, *Ann. Reports*, 1933, **30**, 123). We have therefore investigated the crystal structure of germanous iodide.

Hydrated germanous hydroxide was prepared by a modification of the method of Dennis and Hulse (*J. Amer. Chem. Soc.*, 1930, **52**, 3553), involving reduction of a solution of germanium tetrachloride by hypophosphorous acid at 90° in an atmosphere of nitrogen, and subsequent precipitation of the hydroxide by aqueous ammonia. The hydroxide was filtered off in a nitrogen atmosphere, and dissolved in hot concentrated hydriodic acid from which the free iodine had been removed by warming with the minimum quantity of hypophosphorous acid. On cooling the solution, crystals were obtained in very thin, six-sided plates which were optically uniaxial with fairly strong negative double refraction. They decomposed slowly in air.

Oscillation photographs taken with copper radiation gave for the hexagonal cell size $a = 4·13$, $c = 6·79$ A., and a calculated density for one molecule per unit cell of 5·37. The dimensions, which are near to those required for a hexagonal close-packing of iodine ions, suggest that the structure is the *C*.6 (so-called cadmium iodide type) of Ewald and Hermann's " Strukturbericht." The layer character of the structure is shown by the flakiness of the crystals, the negative double refraction, and certain peculiarities in the X-ray reflexions. Photographs obtained with extremely thin, hexagonal plates oscillated about the *a* axis show moderately sharp *hki*0 reflexions, but *hkil* spots are spread out into streaks along Debye–Scherrer curves. The effect varies from crystal to crystal but sometimes the streaks may reach nearly half way to adjacent layer lines. It may be explained by bending of the crystal, with slipping of the layers of the structure over each other so that, although the normal to a plane 0001 or *hkil* varies in direction from one portion of the crystal to another, there is very little bending of *hki*0 planes.

No weak reflexions that would require an enlargement of the unit cell similar to that found for cadmium iodide by Hassel (*Z. physikal. Chem.*, 1933, *B*, **22**, 333) were observed, but if present they would be very diffuse and difficult to detect. There were no systematic absences of spectra, and the space group may therefore be one of the large number of hexagonal-latticed groups of the trigonal and hexagonal systems satisfying this condition. None of the hexagonal groups will give a structure compatible with intensities and probable interatomic distances, and the others are either excluded on similar grounds or all lead to a *C*.6 structure belonging to the trigonal system.

The inequalities to be expected in relative intensities of certain *hkil* and $hki\bar{l}$ reflexions for a *C*.6 structure were not observed, but the observations are consistent with this structure twinned on the basal plane. For many planes the relative intensities could not be estimated accurately owing to the varying diffuseness of the spots; the general regularities in relative intensity are, however, in good agreement with calculation; *e.g.*, $0h\bar{h}0$ is always very weak unless $h = 3n$, and $hh\bar{2h}0$ is strong for all values of *h*. These data are explained by a cell with Ge at 000 and 2I at $\frac{1}{3}\frac{2}{3}z$ and $\frac{2}{3}\frac{1}{3}\bar{z}$. That *z* is very close to 0·25 is shown by other regularities, and particularly by the relative intensities in the series 000*l* for which calculated and observed values are given in the table.

*Relative intensities of 000l.*

| $l$ | 1. | 2. | 3. | 4. | 5. | 6. | 7. | 8. |
|---|---|---|---|---|---|---|---|---|
| Obs. | m | vs | m | vs | vvw | m | w | ms |
| Calc. | 7·9 | 16·3 | 1·3 | 13·5 | 0·4 | 1·8 | 0·25 | 8·1 |

Each germanium has six iodine neighbours at 2·94 A. from it, arranged octahedrally, and each iodine has three equidistant germanium neighbours at this distance. In this type of structure the binding between atoms in the layers is ionic, but the distance is decreased under the influence of co-ordination number and polarisation forces, and the result therefore provides evidence for the existence of the germanous ion. The Ge–I separation of 2·94 A. is very much greater than the distance 2·57 A. found in the covalent germanium tetraiodide (Jaeger, Terpstra, and Westenbrinck, *Proc. K. Akad. Wetensch. Amsterdam*, 1925, **28**, 747).

An estimate of the radius of the germanous ion as it would be in a sodium chloride type structure may be made from the results as follows. It is assumed that the departure of the germanium–iodine separation in this structure from the sum of the ionic radii (for sodium chloride structures) is the same as in cadmium iodide, *viz.*, a decrease of 7½%, and we therefore obtain for the sum of the germanous and the iodine radius the value 3·18 A. By subtraction of the iodine radius, 2·20 A. (Goldschmidt), the germanous ion radius is found to be 0·98 A.

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## 36. *The Structure of β-(cis-)Diamminoplatinous Chloride : Evidence based on the Preparation of the Palladochloride.*

By F. W. CHATTAWAY and H. D. K. DREW.

β-(*cis*-)Diamminoplatinous chloride gives, with potassium palladochloride, the salt $[Pt(NH_3)_2]PdCl_4$, from which the generators can be re-formed by treatment with an excess of aqueous potassium chloride. Hitherto, the occurrence of a salt of this type has been regarded as impossible, owing to the apparent lack of ionisation of the chlorine atoms of β-diamminoplatinous chloride. The salt may be compared with Magnus's salt, or with its analogue, $[Pt(NH_3)_4]PdCl_4$, and its preparation shows that β-diamminoplatinous chloride possesses potentially ionisable chlorine atoms, the structure *cis*-$Pt(NH_3Cl)_2$ being thus supported. The palladi-salt, $[Pt(NH_3)_2Cl]_2PdCl_6$, has also been prepared, in a nearly homogeneous state. The α- and the γ-form of diamminoplatinous chloride did not react with palladous chloride or potassium palladochloride under the conditions tried; nor did a number of other α- and β-platinammines.

THE structure (I), advocated for β-diamminoplatinous chloride by Drew, Pinkard, Wardlaw, and Cox (J., 1932, 993), has been criticised on the ground that there was little evidence of the tendency towards ionisation of the chlorine atoms which would be expected if they were associated with the nitrogen atoms. This point is met by the assumption of a partial control of the valency electrons of nitrogen by the neighbouring unsaturated platinum atom (*loc. cit.*, p. 998), but it seemed probable that in certain circumstances the ions might become manifest. The object of the present work was to see whether

| $Pt\!<\!\begin{smallmatrix}NH_3Cl\\NH_3Cl\end{smallmatrix}$ | $[Pt(NH_3)_2Cl]_2PdCl_6$ | $[Pt(NH_3)_2]PdCl_4$ |
|---|---|---|
| (I.) | (II.) | (III.) |

β-diamminoplatinous chloride could simulate the behaviour of an admittedly ionised substance, such as $[Pt(NH_3)_4]Cl_2$ or $[Pt(NH_3)_3Cl]Cl$. These substances react with platinous and palladous chlorides or their salts in a well-known manner, of which the formation of Magnus's salt is an example :

$$[Pt(NH_3)_4]Cl_2 + K_2PtCl_4 = [Pt(NH_3)_4]PtCl_4 + 2KCl.$$

Similarly, the triammine gives $[Pt(NH_3)_3Cl]_2PtCl_4$; and the corresponding mixed pallado–plato-salts, *e.g.*, $[Pt(NH_3)_4]PdCl_4$, are readily prepared (Drew, Pinkard, Preston, and Wardlaw, J., 1932, 1896).

On treating palladous chloride in hydrochloric acid with an aqueous solution of β-diamminoplatinous chloride during some days, we obtained small jet-black plates of *bis-*(β-*chlorodiamminoplatinous*) *palladichloride* (II), probably formed by the oxidation in presence of hydrochloric acid of the corresponding palladochloride, $[Pt(NH_3)_2Cl]_2PdCl_4$, a small proportion of which appeared to be associated with it. The palladichloride is decomposed by hot water or hydrochloric acid, or by aqueous potassium chloride, into the original β-platodiammine chloride and chloropalladic acid (or the potassium salt) or its decomposition products. In the circumstances attending the preparation of (II), therefore, β-diamminoplatinous chloride behaves in the same manner as the triammine $[Pt(NH_3)_3Cl]Cl$.

However, when the palladichloride (II) was redissolved by heating in the original mother-liquor, a new salt separated on cooling. This was obtained quite pure and was shown to be β-*diamminoplatinous palladochloride* (III). It formed greyish-black, metallic-looking needles, having a bronzed reflex. With aqueous potassium chloride it was decomposed into its generators, and a similar action took place with hydrochloric acid.

The above reactions with palladous chloride in hydrochloric acid were repeated a number of times under different conditions. They are difficult to carry out, owing to the well-known tendency towards oxidation of the β-platodiammine compounds in the presence of this acid and also to the simultaneous production of both palladous and palladic compounds. It was found, however, that the action of the β-platodiammine on potassium palladochloride gave (III) without complication, the preparation of this substance being thus greatly simplified. In the production of (III), therefore, the β-platodiammine behaves like a platotetrammine, the reaction being reversible :

$$[Pt(NH_3)_2]Cl_2 + K_2PdCl_4 \rightleftharpoons [Pt(NH_3)_2]PdCl_4 + 2KCl.$$

The foregoing reactions of β-diamminoplatinous chloride show that it can behave as if it had either of the formulæ $[Pt(NH_3)_2]Cl_2$ and $[Pt(NH_3)_2Cl]Cl$. Formula (I), which represents the chlorine atoms as being potentially ionisable from the nitrogen atoms, is compatible with both of the above formulæ, either both chlorine atoms or one becoming ionised. An alternative hypothesis would be to regard the chlorine atoms as ionisable from platinum, against which must be set the failure of α-diamminoplatinous chloride and its γ-isomeride to react with palladous chloride, and also their failure to give the reactions (see below) which characterise the β-isomeride. Formulæ showing chlorine co-ordinated with palladium, as $(NH_3)_2Pt\langle{}^{Cl}_{Cl}\rangle PdCl_2$ for (III), appear unlikely, since other β-platodiammines and their α-isomerides should then react in the same way and this is not the case.

It has already been shown (Drew and Wyatt, J., 1934, 56; Saenger and Wardlaw, *ibid.*, p. 182) that β-$Pt(NH_3)_2Cl_2$ has the nitrogen atoms disposed in *cis*-positions about platinum, and that this β-diammine differs from the α- and γ-isomerides in its behaviour in forming (1) Cossa's ammonium salt with hydrochloric acid, (2) the greenish-black diamminodichloroplatosulphuric acid with concentrated sulphuric acid (Drew, J., 1934, 1793), and (3) the purplish-black complex with phenoxtellurine dibisulphate (Drew, *loc. cit.*). The reactions described in the present paper have the same implication, but on account of their simplicity they present the issue in a clearer light.

Finally, it has been pointed out (Drew and Tress, J., 1933, 38; 1935, 1212) that among the β-platodiammine dichlorides there are to be found two types : (*a*) those (*e.g.*, β-Pt $etn_2Cl_2$ and Pt $enCl_2$) which do not give the reactions with hydrochloric acid, sulphuric acid, and phenoxtellurine dibisulphate, and presumably have the chlorine atoms attached to platinum, and (*b*) the much smaller class which show the three reactions to a greater or less extent, and, in at least a proportion of their molecules, have

the chlorine atoms attached to nitrogen. Of the latter class, β-$Pt(NH_3)_2Cl_2$ is the only member so far described which shows each of the reactions in a very pronounced manner, and its character must, therefore, be regarded as somewhat exceptional. A number of β-diammines of the first type were tried, and all failed to react with palladous chloride; several other α-diammines likewise failed to react.

## Experimental.

*Bis-(β-chlorodiamminoplatinous) Palladichloride* (II).—Palladous chloride (5—7 parts by wt.) was dissolved in just sufficient warm concentrated hydrochloric acid, and to the solution was added a saturated solution of β-$Pt(NH_3)_2Cl_2$ (1 part) in boiling water. The mixture was heated to boiling and allowed to cool, with stirring. Part of the β-dichloride separated unchanged, but after about ½ hour voluminous black plates began to separate; after 1—5 days' standing, according to the concentrations used, the whole of the separated material consisted of (II). The above conditions gave a maximum yield, but others may be employed allowing different periods of reaction. If the solutions are too dilute, the reaction occurs over a very protracted period and may be incomplete, and if too much β-diammine is used, part of it is gradually oxidised to β-diamminoplatinous tetrachloride, which forms a troublesome impurity. The following is an example of a favourable mixture: 0·9 g. of palladous chloride in 2·25 c.c. of concentrated hydrochloric acid; 0·15 g. of β-$Pt(NH_3)_2Cl_2$ in 10·5 c.c. of water. When the change was complete, the product was filtered off, washed with 15% hydrochloric acid and then with water, and dried over phosphoric oxide (additional washing with alcohol and ether gave the same result). [The palladous chloride used in the above reactions was obtained by dissolving the metal in concentrated nitric acid, evaporating to dryness, and then evaporating three times with concentrated hydrochloric acid, brownish-black prisms being left.] The *palladichloride* (II) consisted of microscopic jet-black plates, grey or black in bulk, and black when powdered; when contaminated with the β-diammine it appeared greenish-black; if the period of reaction was longer than 7 days, contamination with (III) was liable to occur. When warmed on the water-bath with dilute hydrochloric acid or aqueous potassium chloride, it was decomposed quantitatively into β-$Pt(NH_3)_2Cl_2$ and probably a mixture of pallado- and palladi-chloric acids (or their potassium salts), with partial loss of chlorine; the filtrates from β-$Pt(NH_3)_2Cl_2$ showed chemiluminescence with an alkaline solution of 5-aminophthalaz-1 : 4-dione. When warmed with water, it dissolved and was decomposed in the same manner, a little β-$Pt(NH_3)_2Cl_2$ first separating on cooling, and then long metallic-looking needles of (III) produced by recombination of the remaining constituents. Little or no production of β-$Pt(NH_3)_2Cl_4$ appeared to occur in these decomposition reactions. Numerous analyses of different preparations of (II) were carried out, of which the following may be quoted:

| | Pd + Pt. | Pd. | Pt. | N. | Cl. |
|---|---|---|---|---|---|
| Found (1st sample), % | 57·6 | 12·3 | 45·5 | 7·8 | 29·9 |
| Found (2nd sample), % | 57·9 | 13·15 | 46·05 | 7·5 | 32·25 |
| $H_{12}N_4Cl_8PdPt_2$ requires | 58·5 | 12·55 | 45·95 | 6·6 | 33·45 |

(The determination of Pd + Pt was independent of the separate determinations of Pd and of Pt.) The results for the two samples give the ratios of atoms: N : Cl : Pd : Pt = 4·8 : 7·2 : 1·0 : 2 and 4·5 : 7·7 : 0·9 : 2, respectively, showing that the substance was substantially (II), probably contaminated with a little $[Pt(NH_3)_2Cl]_2PdCl_4$.

β-*Diamminoplatinous Palladochloride* (III).—The second of the following methods of preparation gave a rather better result, since all chance of contamination with β-$Pt(NH_3)_2Cl_4$ was absent: (1) The preparation of (II) was carried out, but the precipitate, instead of being filtered off, was redissolved in the mother-liquor by heating for about ½ min.; on standing, the solution deposited (III) in clusters of needles, which were washed and dried as in the case of (II). (2) A saturated solution of potassium palladochloride (about 6 parts by wt.) in cold water was treated with a solution of β-$Pt(NH_3)_2Cl_2$ (1 part) in boiling water, and the mixture allowed to cool: after some days, long lustrous needles of (III) were produced, which were washed and dried as before. The change was first apparent after about 20 minutes, but reaction was never complete in less than 4 days; with dilute solutions the change was not completed even after long standing. The *palladochloride* (III) formed clusters of greyish-black needles with dark copper-like bronze; when warmed with water or dilute hydrochloric acid, it broke up into β-$Pt(NH_3)_2Cl_2$ and $H_2PdCl_4$, the latter being partly hydroxylated when water was used; partial recombination to (III) took place on standing. With warm aqueous

potassium chloride, reversal of the reaction described under the second method of preparation occurred. The analyses were as follows :

| | Pd + Pt. | Pd. | Pt. | N. | Cl. |
|---|---|---|---|---|---|
| Found (preptn. 1, two samples), % ... | 63·0, 62·95 | 21·85 | 40·15, 40·8 | 6·3 | 31·25, 30·4 |
| Found (preptn. 2), % ..................... | 63·0 | 21·85 | 40·7 | 5·9 | 30·1 |
| $H_8N_2Cl_4PdPt$ requires ..................... | 63·15 | 22·35 | 40·8 | 5·85 | 29·75 |

*Methods of Analysis.*—Pd + Pt was determined by the micro-muffle method. The separate determination of platinum was made by weighing the β-$Pt(NH_3)_2Cl_2$ produced on decomposition of the sample (20—40 mg.) with aqueous potassium chloride (0·5—0·8 c.c.); the separate determination of palladium was made by precipitating the above filtrate from β-$Pt(NH_3)_2Cl_2$ with an excess of a 1% solution of α-dimethylglyoxime in 95% alcohol, the precipitate being thoroughly washed with water to remove any potassium chloride. It was found that the dimethylglyoxime method of precipitating palladium was inaccurate if water or hydrochloric acid was used to decompose either of the substances (II) and (III); but the results were trustworthy in neutral solution, as was shown by comparative trials with potassium palladochloride. Precipitation of the palladium as $[Pt(NH_3)_4]PdCl_4$ gave low resnlts.

We noticed during the present work that potassium palladichloride (but not the palladochloride) produced a momentary chemiluminescence when added to an alkaline solution of 5-aminophthalaz-1 : 4-dione; none of the diamminoplatinous chlorides produced a luminescence in this way; but substance (II) did so, showing that it contains palladic palladium. Potassium platinichloride and both the red and the green form of Pt $etn_4Br_2$ (J., 1935, 1245) gave the above chemiluminescence.

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## 37. *A Modified Grignard Reaction in the Synthesis of Hydrocarbons.*

By J. W. H. OLDHAM and A. R. UBBELOHDE.

Investigation of the products of reaction of butyl, octyl, nonyl, undecyl, dodecyl, tetradecyl, hexadecyl, octadecyl and benzyl halides with magnesium in ether shows that the three reactions

| | | |
|---|---|---|
| (1) | formation of the Grignard reagent | RI + Mg = R·MgI |
| (2) | Wurtz reaction | 2RI + Mg = $R_2$ + $MgI_2$ |
| (3) | disproportionation | 2RI + Mg = RH + R'H + $MgI_2$ |

take place concurrently. The extent to which each reaction takes place depends on the halogen and on the alkyl radical. Repeated addition of iodine, followed by magnesium, leads to yields of 65% or more of the long-chain paraffins $R_2$. The same method of synthesis is even more successful in the case of benzyl halides. Experimental evidence on the mechanisms of the various reactions is discussed, and an improved method of purifying long-chain paraffins is described.

APART from their biological interest, long-chain compounds are of increasing importance in certain physicochemical investigations [for references, see Ubbelohde, *Trans. Faraday Soc.* (in the press)]. On account of difficulties in their purification, it is very desirable, in a study of the physical properties, to prepare long-chain compounds by a number of different synthetic methods. The present paper gives details of the synthesis of the paraffins RH and $R_2$ from the alcohol R·OH. This method can be readily applied in preparing the paraffins $C_{12}H_{26}$, $C_{14}H_{30}$, $C_{16}H_{34}$, $C_{18}H_{38}$, $C_{24}H_{50}$, $C_{28}H_{58}$, $C_{32}H_{66}$, $C_{36}H_{74}$, etc., and thus fills in the gaps left by the Kolbe–Petersen method (cf. Piper, Chibnall, Hopkins, Pollard, Smith, and Williams, *Biochem. J.*, 1931, **25**, 2072), which is only suitable for paraffins such as $C_{22}H_{46}$, $C_{26}H_{54}$, $C_{30}H_{62}$, and $C_{34}H_{70}$. The same method has been investigated for

the benzyl halides, in order to show that it can be applied in the synthesis of any symmetrical hydrocarbon $R_2$. The experiments may be divided into an investigation on the Grignard reaction with a number of halides, and investigations on the synthetic method proposed.

*The Grignard Reaction with Alkyl Halides.*—The method of carrying out the reactions and isolating the products is described in the experimental part. The table summarises experiments designed to give a survey of the whole field, and detailed experiments on dodecyl chloride and iodide, hexadecyl iodide, and benzyl chloride and iodide.

*Extent of Various Reactions Between* n-*Alkyl Halides and Magnesium.*

| Halide. | Grignard compound, %. | Dispropor-tionation, %. | Wurtz reaction, %. | Halide. | Grignard compound, %. | Dispropor-tionation, %. | Wurtz reaction, %. |
|---|---|---|---|---|---|---|---|
| $C_4H_9I$ ........... | — | — | 9·2 | $C_{14}H_{29}I$ ........ | 64·0 | 6·4 | 29·6 |
| $C_8H_{17}I$ ........ | — | — | 25·0 | $C_{16}H_{33}I$ ..... | 64·4 | 8·8 | 27·8 |
| $C_9H_{19}I$ ........ | — | — | 25·0 | $C_{16}H_{33}I$ * ...... | 22·5 | 13·7 | 63·8 |
| $C_{11}H_{23}I$ ........ | — | — | 28·0 | $C_{18}H_{37}I$ ...... | 66·5 | 7·7 | 27·8 |
| $C_{12}H_{25}Cl$ ...... | 91·5 | 3·7 | 4·7 | $C_6H_5{\cdot}CH_2Cl$ ... | 87·5 | — | 9·4 |
| $C_{12}H_{25}I$ ........ | 64·8 | 5·6 | 29·2 | $C_6H_5{\cdot}CH_2I$ ... | 62·0 | — | 38·0 |
| $C_{12}H_{25}I$ * ...... | 15·8 | 20·7 | 62·5 | $C_6H_5{\cdot}CH_2I$ †... | — | — | 68·4 |
| $C_{12}H_{25}I$ ‡ ...... | — | 39·0 | 32·6 | | | | |

* Five additions of iodine and magnesium. † One addition of iodine.
‡ Grignard compound boiled for 6½ hours with an equivalent amount of $C_{12}H_{25}I$.

Attention may be drawn to the following features of this table:

*Relative extent of the Wurtz and the Grignard reaction, etc.* The figures are calculated on the assumptions that all the hydrocarbon $R_2$ is formed by the Wurtz reaction, $2RI + Mg \longrightarrow MgI_2 + R_2$, and that the hydrocarbon RH is formed both from the Grignard compound on addition of dilute hydrochloric acid, $R{\cdot}MgI + HCl \longrightarrow RH + MgICl$, and in the disproportionation reaction, *e.g.*, $2C_{12}H_{25}I + Mg \longrightarrow MgI_2 + C_{12}H_{26} + C_{12}H_{24}$. The basis of these assumptions is discussed below.

The extent to which the iodides from *n*-octyl iodide to *n*-octadecyl iodide undergo the Wurtz reaction only changes from 25 to 28%, and the marked change from butyl to octyl iodide may be connected with the greater facilities for the supply of activation energy in the longer alkyl radicals (cf. Ubbelohde, *Proc. Roy. Soc.*, 1935, *A*, **152**, 362). Special experiments on hexadecyl iodide showed that the proportion of the product formed by the Wurtz reaction is not greatly affected by changes in the mode of addition of halide to the system, and that the volume of ether used cannot be much varied without leading to inconvenience of manipulation. Benzyl iodide shows a somewhat greater proportion formed by the Wurtz reaction, for reasons discussed below.

It follows from this table that the chloride should be used whenever the Grignard compound is intended for further syntheses, since this involves the minimum loss of halide in the Wurtz reaction (cf. also Johnson and Adkins, *J. Amer. Chem. Soc.*, 1932, **54**, 1944; Zoellner, *Chem. Abstracts*, 1935, **29**, 5413).

*Mechanism of the Wurtz reaction and of the formation of unsaturated compounds.* In addition to the Grignard and the Wurtz reaction, the halides react to the extent of 4—8% to give unsaturated hydrocarbons of the same chain length as the alkyl radical. Information on the mechanism of both this reaction and the Wurtz reaction is obtained from experiments on the effect of prolonged boiling of excess of dodecyl iodide or benzyl iodide with the corresponding Grignard compound. In the case of dodecyl iodide, it will be seen from the table that in 6½ hours the extent of the Wurtz reaction is hardly affected, whereas the amount of disproportionation is increased sevenfold. Since the total time of interaction of dodecyl iodide with the Grignard compound is as much as twenty-five times as long in this experiment as in the primary interaction with magnesium, it is clear that the Wurtz reaction does *not* proceed by the mechanism $RI + R{\cdot}MgI \longrightarrow MgI_2 + R_2$, whereas disproportionation depends to an important extent on the reaction $C_{12}H_{25}I + C_{12}H_{25}{\cdot}MgI \longrightarrow MgI_2 + C_{12}H_{24} + C_{12}H_{26}$, which may involve the temporary formation of free radicals in solution (cf. Späth, *Monatsh.*, 1913, **34**, 1978; Gilman and Fothergill, *J. Amer. Chem. Soc.*, 1928, **50**, 3334).

The benzyl halides show a marked contrast with the alkyl halides in this respect. When benzylmagnesium chloride was boiled with an equivalent amount of benzyl iodide for 10 minutes, the reaction (*A*) $C_6H_5{\cdot}CH_2I + C_6H_5{\cdot}CH_2{\cdot}MgCl \longrightarrow MgClI + (C_6H_5{\cdot}CH_2)_2$ took place to the extent of 87·5% of the theoretical.

*Use of the Results in the Wurtz Synthesis of Hydrocarbons.*—The unsatisfactory yield of hydrocarbon $R_2$ obtained when sodium is used with the higher alkyl halides is probably connected with the disproportionation reaction. In the action of alkyl halides on magnesium, the data show this to be relatively unimportant compared with the Wurtz reaction. A synthesis which does not waste the large amounts of Grignard compound formed at the same time (cf. Levene, West, and v. der Scheer, *J. Biol. Chem.*, 1915, **20**, 521) is possible as follows: The alkyl iodide is first allowed to react with magnesium under standard conditions, leading to about 25% of product formed by Wurtz reaction. An amount of iodine is now added equivalent to the Grignard compound formed, the reaction being assumed to be $I_2 + R{\cdot}MgI \longrightarrow RI + MgI_2$. The requisite amount is calculated from a blank reaction, or by cautiously adding iodine till the colour persists. A fresh amount of magnesium is added to react with the alkyl iodide recovered, and the sequence of operations is repeated till a sufficient yield of $R_2$ has accumulated to make isolation profitable. Although the yield of product formed by the Wurtz reaction decreases in geometric proportion in the successive interactions with magnesium, it cannot be brought to 100% by indefinite addition of iodine and magnesium, owing to the concurrent loss of alkyl halide by the disproportionation reaction. Yields of 65% can be obtained by a series of five additions of iodine and magnesium. This compares very favourably with any other method of making long-chain paraffins, both in the yield and in the purity of the products.

Although magnesium only acts slowly on iodine in ether, the simultaneous addition of iodine and an alkyl iodide to magnesium was not found to be as satisfactory as the alternate addition of iodine and magnesium to the Grignard compound.

*Mechanism of the Action between Iodine and Grignard Compounds.*—The fact that no other reaction of importance has been missed in the interaction between alkyl compounds and magnesium may be verified as follows: Suppose that, in a single addition of alkyl halide to magnesium, the three competing reactions

$$RI + Mg \longrightarrow R{\cdot}MgI$$
$$RI + \tfrac{1}{2}Mg \longrightarrow \tfrac{1}{2}R_2 + \tfrac{1}{2}MgI_2$$
$$RI + \tfrac{1}{2}Mg \longrightarrow \tfrac{1}{2}[RH + R'H] + \tfrac{1}{2}MgI_2$$

take place to the extent $x$, $y$, and $1 - (x + y)$ respectively. If the addition of iodine to the product leads to the re-formation of alkyl iodide wholly by the reaction $I_2 + R{\cdot}MgI \longrightarrow RI + MgI_2$, the fraction $x$ of the original alkyl iodide will be re-formed. In the next addition of magnesium, the hydrocarbons now present being assumed not to affect the relative extent of the three reactions, the fraction of Grignard compound formed will be $x^2$, and the total yield produced by the Wurtz reaction, $y + xy$. After five additions of iodine and magnesium, the total yield of $R_2$ according to these assumptions will be $y(1 + x + x^2 + x^3 + x^4)$ or, in the case of dodecyl iodide, $0{\cdot}29(1 + 0{\cdot}65 + 0{\cdot}42 + 0{\cdot}27 + 0{\cdot}18) = 73{\cdot}0\%$, which compares with a found yield of 62·5%. For hexadecyl iodide the corresponding figures are: theoretical yield, 69·5%; found, 63·8%. Further evidence on the action of iodine on the Grignard compounds is obtained as follows:

*Action of iodine on the compounds* R·MgCl. In these experiments the alkylmagnesium chloride was formed in the usual way; the theoretical amount of iodine for complete decomposition of the Grignard compound was slowly added, and finally the products were separated by addition of dilute hydrochloric acid and fractionation and analysed.

From a comparison of the yield in blank experiments with the yields of various products, the following reactions take place on the addition of iodine to dodecylmagnesium chloride:

$$(1)\ C_{12}H_{25}{\cdot}MgCl + I_2 \longrightarrow MgICl + C_{12}H_{25}I \quad 71{\cdot}0\%$$
$$(2)\ C_{12}H_{25}{\cdot}MgCl + I_2 \longrightarrow MgI_2 + C_{12}H_{25}Cl \quad 16{\cdot}4\%$$
$$(3)\ C_{12}H_{25}{\cdot}MgCl + \tfrac{1}{2}I_2 \longrightarrow \tfrac{1}{2}C_{24}H_{50} + MgICl \quad 5{\cdot}1\%$$
$$(4)\ C_{12}H_{25}{\cdot}MgCl + \tfrac{1}{2}I_2 \longrightarrow \tfrac{1}{2}(C_{12}H_{26} + C_{12}H_{24}) + MgICl \quad 4{\cdot}3\%$$

*The points of interest in this result are:*

(a) Dodecylmagnesium chloride reacts at least partly in this form, and not wholly as $Mg(C_{12}H_{25})_2 + 2I_2 \longrightarrow MgI_2 + 2C_{12}H_{25}I$, which might be possible according to the results of Schlenk and Schlenk (*Ber.*, 1929, **62**, 920; 1931, **64**, 734) if the equilibrium $2C_{12}H_{25}{\cdot}MgCl \rightleftharpoons Mg(C_{12}H_{25})_2 + MgCl_2$ is sufficiently displaced to the right.

(b) Chlorides may be used equally well in the synthesis of $R_2$.

(c) Reaction (3), which may possibly proceed as

$$Mg(C_{12}H_{25})_2 + I_2 \longrightarrow MgI_2 + C_{24}H_{50}$$

only takes place to the extent of 5·1%.

This contrasts with the behaviour of benzyl chloride, in which the reactions are

(1) $C_6H_5{\cdot}CH_2{\cdot}MgCl + I_2 \longrightarrow MgICl + C_6H_5{\cdot}CH_2I$ 8·7%
(2) $C_6H_5{\cdot}CH_2{\cdot}MgCl + I_2 \longrightarrow MgI_2 + C_6H_5{\cdot}CH_2Cl$ 10·2%
(3) $C_6H_5{\cdot}CH_2{\cdot}MgCl + \frac{1}{2}I_2 \longrightarrow \frac{1}{2}(C_6H_5{\cdot}CH_2)_2 + MgICl$ 80·0%.

Reaction (3) in this case most probably proceeds as shown in (*A*) (p. 203). (For the addition of other halogens to Grignard compounds, see Datta and Mitter, *J. Amer. Chem. Soc.*, 1919, **41**, 282.)

*Purification of Long-chain Paraffins.*—A method of purifying paraffins has been described by Piper *et al.* (*loc. cit.*), according to which the paraffin is heated with concentrated sulphuric acid at 130° till no more charring is observed during 2 hours. Blank experiments on the rate of removal of added cetene ($C_{16}H_{32}$), and alkyl halides, showed that a very much more rapid purification could be effected by heating the paraffins with 20% oleum at 100° till the test for halide was negative, followed by a short treatment with concentrated sulphuric acid at 130° to remove any sulphonic acids formed. Owing to the appreciable oxidation of certain liquid paraffins at 130° it is advisable to hinder the circulation of air over the surface of the paraffin during the purification.

After treatment with sulphuric acids the paraffins are washed, dried, and distilled in a vacuum. Mixed melting points are of little use in estimating the purity of paraffins, but *X*-ray and calorimetric measurements [Ubbelohde, *Trans. Faraday Soc.* (in the press)] showed that paraffins prepared and purified by the methods described here were of the highest purity yet obtained.

## EXPERIMENTAL.

As the work was largely concerned with homologous or closely similar compounds, it is sufficient to give details of a limited number of experiments.

*Dodecyl Chloride* (Schuchardt, b. p. 132—134°/18 mm.).—To 1·2 g. of magnesium in 40 c.c. of ether, 10·2 g. of the chloride and one crystal of iodine were added; the mixture was kept for at least 30 minutes in the cold, and the reaction then completed by 3 hours' boiling under reflux with protection from atmospheric moisture. After addition of dilute hydrochloric acid, washing with water, sodium thiosulphate solution and again with water, drying at 100°/25 mm., and fractionation, the total yield was 8·35 g. On distillation at 18 mm., 7·90 g. distilled, leaving a residue of much higher b. p., the amount of which (0·4 g.) was too small for analysis for halogen content. The distillate contained 0·4% of chlorine (Stepanov's method) and 1·9% of dodecene, determined by adding bromine in carbon tetrachloride and estimating the excess iodometrically after 1 hour.

*Addition of iodine to dodecylmagnesium chloride.* To the Grignard compound formed as above (9·2 g. of the chloride, 37 c.c. of ether, and 1·1 g. of magnesium), 12 g. of iodine were slowly added, the mixture being kept cool. The colour faded instantly for the first 10 g., then more slowly. The solution was boiled for 5 minutes to complete the reaction, and dilute hydrochloric acid added before the products were isolated as above. The total product was 11·92 g., of which 10·97 g. distilled below 180°/18 mm., leaving a high-boiling residue (0·91 g.).

The distillate was analysed for total halogen by Stepanov's method, and the relative amounts of chloride and iodide were determined by using a known excess of silver nitrate in precipitating the halides, and determining the excess. The distillate contained 2·67% of chlorine, 33·0% of iodine, and 0·29% of unsaturated hydrocarbon, the rest being saturated hydrocarbon. The residue contained 11·5% of iodine, which could be separated as a volatile iodide on redistillation.

*Dodecyl Iodide.*—This was prepared from dodecyl alcohol (Schuchardt) by heating at 140° for 3 hours with 10% more than the theoretical quantities of red phosphorus and iodine; the product was cooled, dissolved in ether, washed with 10% sodium hydroxide solution and with water, dried, and distilled in a vacuum (b. p. 159—160°/15 mm.). To 80 c.c. of ether and 1·8 g. of magnesium, 20·7 g. of the iodide were added in 15 minutes. After addition of dilute hydrochloric acid, the total product isolated was 12·1 g., with 3·7 g. of high-boiling residue after distillation. The unchanged iodide was determined by Stepanov's method, the residue containing 2·1%, and the distillate 1·3% of iodine. The unsaturated hydrocarbon in the distillate corresponded with 4% of dodecene. A small amount of unsaturated substances in the residue was investigated in more detail in the case of hexadecyl iodide (below).

*Repeated addition of iodine.* After preparation of the Grignard compound as above (15·3 g. of the iodide, 60 c.c. of ether, and 1·3 g. of magnesium), alternate additions were made of the following amounts of iodine, 9·7, 7·0, 5·0, 4·0, and 3·0 g., and the following amounts of magnesium, 0·9, 0·7, 0·6, 0·5, and 0·4 g. The iodine was added slowly with cooling, and the mixture was boiled for 5 minutes before the next addition of magnesium and for 15 minutes before the next addition of iodine. A double layer of liquid was formed owing to the salting-out effect of magnesium iodide. The total product was 8·9 g., of which 5·8 g. did not distil below 180°/18 mm. The residue contained 1·2% of iodine, and 1·5% of unsaturated substances, calculated on the basis of $C_{24}H_{48}$. The distillate contained 17·2% of dodecene.

*Action of dodecyl iodide on dodecylmagnesium iodide.* The Grignard compound was prepared as above (15·6 g. of the iodide, 60 c.c. of ether, and 1·3 g. of magnesium), 15·7 g. of dodecyl iodide added, and the whole boiled for 6½ hours (reflux condenser; calcium chloride guard-tube). On isolation the total product was 21·7 g. Distillation left 3·8 g. containing 9·8% of iodine and 2·9 g. of hydrocarbon. The distillate contained 9·25 g. of hydrocarbon, 20·8% of iodine, and 9·9% of unsaturated hydrocarbon (calculated on the basis of $C_{12}H_{24}$). The residue contained 0·1 double bond per mole of $C_{24}H_{50}$, calculated on the bromine absorption.

*Hexadecyl Iodide.*—The experiments with this iodide were parallel to those with the other iodides, the only special feature being an attempt to determine the nature of the unsaturated substance in the residue. Only one experiment need be described.

*Repeated addition of iodine.* The Grignard compound was formed as above from 20·3 g. of the iodide, 80 c.c. of ether, and 2·1 g. of magnesium. Five additions of iodine, 7·5, 5·8, 4·3, 3·2, and 2·4 g., alternating with 1·4, 1·1, 0·8, 0·6, and 0·4 g. of magnesium, were made as above. The total product was 13·0 g., with 8·3 g. of high-boiling residue (18 mm.). The unsaturation in the distillate, calculated on the basis of $C_{16}H_{32}$, was 19%. The unsaturation in the residue was 0·054 double bond per mole of $C_{32}H_{66}$. This residue, recrystallised from benzene, gave 70% of dotriacontane, $C_{32}H_{66}$, m. p. 71—72°, with no absorption of bromine; the mother-liquor on evaporation gave a pasty yellow mass, which contained 0·2 double bond per mole of $C_{32}H_{66}$. The amount present is practically the same as in a single addition of hexadecyl iodide to magnesium, so the process leading to its formation is not an important part of the reaction between alkyl iodides and magnesium.

*Benzyl Halides.*—These were treated in a precisely similar manner to the alkyl halides, the only difference being that no determination of the disproportionation reaction, if any, could be made. The high-boiling residue was shown to be mainly dibenzyl by the mixed melting point method, but the possibility of the presence of small amounts of other hydrocarbons was not excluded.

*Identification of Paraffins, Blank Experiments, etc.*—The lower paraffins were identified by their b. p.'s and their resistance to the action of concentrated sulphuric acid at 130°, and the higher paraffins by their m. p.'s and resistance to sulphuric acid. Mixed melting points are of little use as a test of the freedom of the products from homologues, but *X*-ray and calorimetric investigations of octadecane obtained from *n*-nonyl alcohol showed that any impurity did not exceed 1%, which compares very favourably with the purity of paraffins made by the electrolysis of the potassium salts of fatty acids.

In the estimation of the relative extent of the Wurtz and the Grignard reaction taking place when an alkyl iodide is added to magnesium, the separation of the product into a high- and a low-boiling fraction becomes somewhat unsatisfactory as the chain length increases, owing to the fact that in the vapour-pressure equation $\ln p = -\lambda/RT + B$ the increase in the latent heat $\lambda$ with chain length is partly compensated by the increase in the constant term $B$ (cf. Ubbelohde's data, *Trans. Faraday Soc.*, *loc. cit.*). A check on the efficiency of separation was made by redistilling a mixture of hexadecane and dotriacontane, and showed that the probable error in the yields given for these substances is not more than 4%. A further check was obtained from

the reproducibility of the yields when the experiments were repeated. Distillation of a mixture of cetene and dotriacontane showed that the former behaved in a similar manner to hexadecane, as might have been expected. The absorption of bromine observed for the crude dotriacontane cannot be wholly due to traces of cetene, in view of this result, but was not further investigated on account of the small amounts available.

The method of analysis of the halides was checked on dodecyl chloride (Found: Cl, 17·7. Calc., 17·3%) and on octadecyl iodide (Found: I, 35·0. Calc., 33·7%). The method of estimation of unsaturated substances was checked on a known mixture of cetene, iodide, and paraffin containing 4·0% of cetene (Found, 4·2%).

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LONDON, W. 1. [*Received, December 20th,* 1937.]

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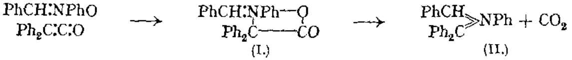
# 38. *The Structure of the "Nitrenes."*

By T. W. J. TAYLOR, J. S. OWEN, and D. WHITTAKER.

The "nitrenes" are a group of compounds first prepared by Staudinger and Miescher; they have been allotted a structure which involves a pentacovalent nitrogen atom. The experiments described here indicate that this structure is erroneous and that they are ethyleneimine derivatives. Hence these compounds do not form an exception to the general rule that the maximum covalency of nitrogen in its compounds is four.

IT is now generally accepted that in its compounds nitrogen shows a maximum covalency of four and that the "pentavalent" nitrogen compounds are either of the type $[NR_4]^+X^-$, where the fifth group is an anion and the fifth valency an electrovalency, or of the type $R_3N \rightarrow O$, in which the bond between nitrogen and oxygen is not a true double bond of four electrons, but a co-ordinate link (semipolar double bond) of two electrons, so that the number of valency electrons held by the nitrogen atom is eight and not ten. There remain, however, in the literature a few compounds for which structures involving pentacovalent nitrogen have been proposed, and where the evidence as stated indicates that they may form exceptions to this generalisation. Such a class is the "nitrenes" of Staudinger and Miescher (*Helv. Chim. Acta*, 1919, **2**, 554; Thesis, Zurich, 1918), but the observations recorded in this paper suggest that they do not possess the constitution which Staudinger and Miescher postulated.

The "nitrenes" are formed by heating the addition compounds of a keten and the *N*-ether of an oxime (a nitrone in Staudinger's nomenclature), and the only ones that can be prepared contain a phenyl group attached to the nitrogen atom and phenyl groups attached to the carbon atoms. An example is "triphenyl-*N*-phenylnitrene" (Staudinger and Miescher, *loc. cit.*); diphenylketen and *N*-phenylbenzaldoxime give an addition compound, which they formulate as (I), and this loses carbon dioxide at 215° to give the nitrene, which they show as (II).



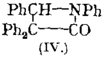
(I.) (II.)

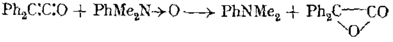
Both the addition compound and the final product were given formulæ which involve pentacovalent nitrogen, but no evidence was advanced in favour of structure (I). As to the structure of the nitrene, Staudinger and Miescher admit the possibility of the ethyleneimine structure (III), but preferred (II) for two reasons. First, they state that the compounds are yellow, while nearly all ethyleneimines are colourless, and secondly, reduction of "tetraphenyl-*N*-phenylnitrene" gave an amine which, it was stated, would not form a nitrosoamine and hence was tertiary; they also state that this amine is identical with

dibenzhydrylaniline, although they had difficulty in synthesising this amine and give no analytical data for their synthetic product.

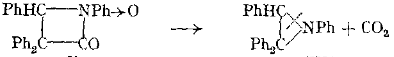
$$\begin{matrix}Ph_2C \\ Ph_2C\end{matrix}\!\!>\!NPh \longrightarrow \begin{matrix}Ph_2CH \\ Ph_2CH\end{matrix}\!\!>\!NPh$$

Apart from the valency difficulty implicit in the structures (I) and (II), the formula (I) for the addition compound seems highly improbable. It is known that a keten will add to a true double bond, but not to the semipolar double bond of an amine oxide; thus Staudinger has shown (*Ber.*, 1907, **40**, 1147) that diphenylketen gives an addition compound with benzylideneaniline and has proved that it has the structure (IV), while he has also shown that with dimethylaniline oxide there is no addition and that diphenylketen oxide is the product.


(IV.)



Hence the addition of a keten to an *N*-phenyl oxime is much more likely to give the trimethyleneimine derivative (V). In such a compound a bond has been established between two carbon atoms, and when carbon dioxide is lost on heating, it is improbable that this bond will disappear. Consequently the "nitrene" is almost certain to contain this bond intact and to be the ethyleneimine (III).


(V.) (III.)

This view, which removes the valency anomalies in (I) and (II), finds support in the following observations. "Triphenyl-*N*-phenylnitrene" has been prepared and its properties are found to correspond with those given by Staudinger and Miescher with two exceptions. It is a colourless compound when pure and, contrary to their statement, it can be easily reduced to an amine. This is undoubtedly a secondary amine, because its *nitroso*-derivative has been obtained and analysed. Hence there is little doubt that the "nitrene" is in reality 1 : 2 : 3 : 3-tetraphenylethyleneimine and that the reaction has proceeded as is shown above. Reduction of the "nitrene" gives only one product, although the two C–N bonds are not identical and their opening should give two different amines. It would be expected that the bond which is less sterically hindered would be attacked the more readily (as shown in the dotted line in III) and the product should be *1-anilino-1 : 1 : 2-triphenylethane*, $NHPh{\cdot}CPh_2{\cdot}CH_2Ph$. This prediction seems to be verified by the fact that Bergmann and Rosenthal (*J. pr. Chem.*, 1932, **135**, 267) have prepared the isomeric 1-anilino-1 : 2 : 2-triphenylethane, $NHPh{\cdot}CHPh{\cdot}CHPh_2$, and find that it melts at 164—166°, whereas our amine melts at 152—153°.

The structure of this "nitrene" would be best established by an independent synthesis, but our many attempts to achieve this have been unsuccessful. *1-Chloro-2-anilino-1 : 1 : 2-triphenylethane*, $CPh_2Cl{\cdot}CHPh{\cdot}NHPh$, has been obtained, but no conditions could be found under which the ethyleneimine ring would close; the chlorine atom resembles that in triphenylmethyl chloride and is extremely readily hydrolysed. The failure to effect ring closure is due to the presence of the two phenyl groups on the carbon atom which carries the chlorine, because we find that *1-chloro-2-anilino-1 : 2-diphenylethane* gives *1 : 2 : 3-triphenylethyleneimine* when heated with alcoholic potash. A similar difficulty is recorded recently by Mannich and Baumgarten (*Ber.*, 1937, **70**, 210) in the closure of the trimethyleneimine ring. Attempts were made to prepare this ethyleneimine by the "nitrene" method from phenylketen and *N*-phenylbenzaldoxime; this would settle the point by showing that a "nitrene" obtained by Staudinger's method was really an ethyleneimine; they were, however, unsuccessful. The formation of ethyleneimines by the thermal decomposition of these addition compounds seems to be conditioned in some unknown way by the presence of several phenyl groups. A further example of this fact was found in the behaviour

of the addition *compound* of diphenylketen and *N*-methylbenzophenoneoxime, which Staudinger was unable to prepare; when heated, this compound does not decompose smoothly to give an ethyleneimine, as the corresponding *N*-phenyl compound does, but only yields an intractable tar.

## Experimental.

*N*-Phenylbenzaldoxime was obtained from *N*-phenylhydroxylamine and benzaldehyde (Bamberger, *Ber.*, 1894, **27**, 1556), and diphenylketen by the thermal decomposition of benzoylphenyldiazomethane (Schroeter, *Ber.*, 1909, **42**, 2346), prepared by the oxidation of benzilmonohydrazone (Curtius and Thun, *J. pr. Chem.*, 1891, **44**, 182). (The oxidation proceeds very much more readily if the yellow mercuric oxide is exposed to the moist air of the laboratory for 24 hours before use.) The decomposition of the diazo-compound was carried out in benzene solution in an atmosphere of carbon dioxide at 50—55°; after 1 hour evolution of nitrogen ceased; the benzene was removed at 60°, and the keten distilled in carbon dioxide; b. p. 146°/12 mm. *N*-Methylbenzophenoneoxime was obtained by methylation of the oxime and separation of the *O*- and the *N*-ether with light petroleum (Semper and Lichtenstadt, *Ber.*, 1918, **51**, 933).

*Addition of Diphenylketen to* N-*Methylbenzophenoneoxime*: 2-*Keto*-3 : 3 : 4 : 4-*tetraphenyl*-1-*methyltrimethyleneimine Oxide*.—The oxime-ether in benzene was added to a benzene solution of its equivalent of the keten in an atmosphere of carbon dioxide; addition of light petroleum precipitated a colourless *compound* which, after several recrystallisations from ligroin–benzene, melted at 164° (Found: C, 82·9; H, 5·8. $C_{28}H_{23}O_2N$ requires C, 83·0; H, 5·7%). The compound decomposed vigorously at 180° and evolved carbon dioxide, leaving a dark tar.

*Addition of Diphenylketen to* N-*Phenylbenzaldoxime*: 2-*Keto*-1 : 3 : 3 : 4-*tetraphenyltrimethyleneimine Oxide*.—The reaction was carried out as described by Staudinger and Miescher (*loc. cit.*); the product purified by washing with ether, light petroleum, and benzene melted at 199—200°; Staudinger and Miescher give m. p. 186—190°. Heating this compound gave "triphenyl-*N*-phenylnitrene" (1 : 2 : 2 : 3-tetraphenylethyleneimine), which after four recrystallisations from alcohol and one from light petroleum with 5% of benzene formed colourless needles, m. p. 107·5°; Miescher described this compound as pale yellow, m. p. 105—106° (Found: C, 89·6; H, 6·05. Calc. for $C_{26}H_{21}N$: C, 89·9; H, 6·05%).

*Reduction of* 1 : 2 : 2 : 3-*Tetraphenylethyleneimine*.—The imine (8 g.) in ether with 1 c.c. of water was treated with freshly prepared aluminium amalgam (5 g.). After 12 hours removal of the ether from the filtered solutions gave 1-*anilino*-1 : 1 : 2-*triphenylethane*, which was recrystallised from aqueous alcohol and ligroin–benzene; yield 7 g., m. p. 152—153° (Found: C, 89·7; H, 6·6. $C_{26}H_{23}N$ requires C, 89·4; H, 6·6%). This amine (1·5 g.) was dissolved in 15 c.c. of alcohol and 5 c.c. of concentrated hydrochloric acid, and a slight excess of saturated aqueous potassium nitrite added at 0°. After 3 hours the sticky solid which separated was collected and recrystallised, first from aqueous alcohol and then from ligroin–benzene; 1 g. of the *nitrosoamine* was obtained, m. p. 114—115° (Found: C, 82·7, H, 6·0; N, 7·3. $C_{26}H_{22}ON_2$ requires C, 82·5; H, 5·8; N, 7·4%).

2-*Anilino*-1 : 1 : 2-*triphenylethyl Alcohol*.—Desylaniline (27 g.) (Cameron, *Trans. Roy. Soc. Canada*, 1929, **23**, 53) in 100 c.c. of ether was added to a solution of phenylmagnesium bromide made from 64 g. of bromobenzene. After 30 minutes on the steam-bath, the mixture was cooled, and ice and concentrated aqueous ammonium chloride added. The ethereal layer gave 17 g. of the *product*, which was recrystallised from alcohol; m. p. 173° (Found: C, 85·3; H, 6·3; N, 3·9. $C_{26}H_{23}ON$ requires C, 85·5; H, 6·3; N, 3·8%).

Replacement of the hydroxyl group by chlorine offered great difficulty; this was traced to the solubility of the hydrochloride of the chloro-compound in chloroform and the extreme ease with which the chloro-compound is hydrolysed to the alcohol. 1-*Chloroanilino*-1 : 1 : 2-*triphenylethane* was eventually obtained by treating the alcohol (15 g.), dissolved in the minimum of ethylene dibromide, with phosphorus pentachloride (9 g.). A white precipitate of the hydrochloride of the compound slowly separated; it was removed and washed with dry ether; yield 8 g.; no definite m. p. Treatment of this hydrochloride with any aqueous reagent or with alcoholic potash regenerated the alcohol. The free base could, however, be obtained by rubbing the hydrochloride with cold dry pyridine; the base was recrystallised from chloroform–light petroleum; m. p. 196° (Found: Cl, 9·5. $C_{26}H_{22}NCl$ requires Cl, 9·3%). Attempts to bring about ring closure with pyridine, quinoline or dimethylaniline were unsuccessful; the product obtained under any conditions gave the alcohol when treated with water, which showed that the chloro-compound was unchanged. Ring closure of the alcohol to the ethyleneimine by heating

with phosphoric oxide in boiling xylene was also tried; the only product isolated was ωω-diphenylacetophenone (m. p. 136°). This would be expected as the hydrolysis product of the anil formed by loss of water from the alcohol:

$$HO{\cdot}CPh_2{\cdot}CHPh{\cdot}NHPh \longrightarrow CPh_2{:}CPh{\cdot}NHPh \longrightarrow CHPh_2{\cdot}CPh{:}NPh \longrightarrow CHPh_2{\cdot}COPh$$

1 : 2 : 3-*Triphenylethyleneimine*.—Desylaniline was reduced to 2-anilino-1 : 2-diphenylethyl alcohol (Voigt, *J. pr. Chem.*, 1886, **34**, 13). This alcohol (3 g.) was treated in 10 c.c. of dry chloroform with phosphorus pentachloride (2·5 g.) and cooled; a hydrochloride (2·8 g.) separated on standing and was treated with excess of cold alcoholic potash. Addition of water precipitated 1-*chloro-2-anilino-1 : 2-diphenylethane*, which was recrystallised from methyl alcohol; m. p. 126° (Found: Cl, 11·5. $C_{20}H_{18}NCl$ requires Cl, 11·5%). When this compound was boiled with an excess of alcoholic potash for 1 hour, the solution turned yellow and potassium chloride separated. Addition of water gave a sticky solid, which was extracted with ether. From this solution a yellow gum was obtained which on recrystallisation gave the *triphenylethyleneimine* in colourless needles, m. p. 99° (Found: N, 5·1. $C_{20}H_{17}N$ requires N, 5·2%).

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## 39. *Aliphatic Substitution and the Walden Inversion. Part III. Comparison, using Radioactive Bromine, of the Rates of Inversion and Substitution in the Reaction of Bromide Ions with α-Bromopropionic Acid.*

By W. A. COWDREY, E. D. HUGHES, T. P. NEVELL, and C. L. WILSON.

The rates of racemisation and of exchange in the reaction of α-bromopropionic acid with lithium bromide, containing a proportion of radioactive bromine, have been measured in acetone solution at 22°. The results show that in the system studied substitution is accompanied by inversion.

SUBSTITUTION theories which have been developed in recent years (cf. Parts I and II, J., 1935, 1525; 1936, 1173; Cowdrey, Hughes, Ingold, Masterman, and Scott, J., 1937, 1252) predict that reactions of type (A), involving the attack of a negative ion on a saturated carbon atom, are accompanied by an inversion of configuration:

$$Y^- + R{-}X \longrightarrow Y{-}R + X^- \quad . \; . \; . \; . \; . \; . \; . \quad (A)$$

In Parts I and II (*locc. cit.*) a direct demonstration of the correctness of this view was obtained in the case of two simple organic halides containing, besides the halogen, only hydrogen and alkyl or aryl groups at the seat of substitution. The method consisted of a comparison of the rate of substitution in the presence of the corresponding halide ions containing a proportion of a radioactive isotope with the rate of racemisation of the optically active halide under comparable conditions, and the replacement of halogen by halogen was shown essentially to involve inversion.

In recent publications from these laboratories (cf. especially Ingold *et al.*, *loc. cit.*) an attempt has been made to relate the steric orientation of substitution with the structure of the reactants and the conditions of reaction. Homogeneous nucleophilic substitutions being treated as either unimolecular ($S_N1$) or bimolecular ($S_N2$), it was shown that, although unimolecular substitution may involve inversion, racemisation or retention of form, depending, *inter alia*, on the nature of the groups attached to the seat of reaction, yet bimolecular substitution invariably leads to inversion. Of the structures examined in this connection, various modifications of the carboxyl group proved to be of the greatest interest. We have therefore examined the reaction between α-bromopropionic acid and lithium bromide in anhydrous acetone solution by the method indicated above.

Our object was to compare the bimolecular rate constants for inversion and exchange, obtained under the same experimental conditions. For inversion this constant ($k_I$) is given by the equation $k_I = 1/2\,Bt \,.\, \log_e \alpha_0/\alpha_t$, where $B$ is the concentration of the lithium

bromide, and $\alpha_0$ and $\alpha_t$ are the optical rotations of the organic acid at zero time and time $t$ respectively. To analyse the substitution data in a comparable manner it is necessary to assume that the bromine isotopes are chemically equivalent. Exchange is then the sum total of the simultaneous reactions (1)—(4), each governed by an identical bimolecular constant $k_E$ (radioactivity is designated by an asterisk).

$$(1)\ \mathrm{RBr} + \mathrm{Br}^- \longrightarrow \mathrm{RBr} + \mathrm{Br}^- \qquad (2)\ \mathrm{RBr} + \overset{*}{\mathrm{Br}}{}^- \longrightarrow \mathrm{R}\overset{*}{\mathrm{Br}} + \mathrm{Br}^-$$

$$(3)\ \mathrm{R}\overset{*}{\mathrm{Br}} + \mathrm{Br}^- \longrightarrow \mathrm{RBr} + \overset{*}{\mathrm{Br}}{}^- \qquad (4)\ \mathrm{R}\overset{*}{\mathrm{Br}} + \overset{*}{\mathrm{Br}}{}^- \longrightarrow \mathrm{R}\overset{*}{\mathrm{Br}} + \overset{*}{\mathrm{Br}}{}^-$$

If we represent the concentration of $\overset{*}{\mathrm{Br}}{}^-$ after time $t$ by $x$, we may write (since throughout the reaction, $[\mathrm{RBr}] + [\mathrm{R}\overset{*}{\mathrm{Br}}] = [\mathrm{Br}^-] + [\overset{*}{\mathrm{Br}}{}^-] = B$)

$$-\,dx/dt = k_E\{[\mathrm{RBr}][\overset{*}{\mathrm{Br}}{}^-] - [\mathrm{R}\overset{*}{\mathrm{Br}}][\mathrm{Br}^-]\} = k_E B(2x - x_0)$$

where the suffix zero refers to the start of the reaction. Integration gives

$$k_E = -\,1/2\,Bt\,.\,\log_e\,(2x/x_0 - 1)$$

The technique which we adopted directly measured $x/x_0$, and in Table I we give the exchange data and the corresponding constants ($k_E$).

TABLE I.

*Bimolecular velocity coefficient* ($k_E$) *for the exchange of radioactive halogen ions with α-bromopropionic acid at* 22° (B = 0·333M).

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Time (mins.) | 20 | 20 | 30 | 30 | 40 | 50 | 60 | 60 |
| $x/x_0$ | 0·846 | 0·854 | 0·761 | 0·737 | 0·726 | 0·660 | 0·642 | 0·662 |
| $10^4 k_E$(sec.$^{-1}$ g.-mol.$^{-1}$ l.) | 4·62 | 4·32 | 5·43 | 6·22 | 4·97 | 5·72 | 5·25 | 4·69 |

The average value of $k_E$ is $5{\cdot}15 \times 10^{-4}$ (sec.$^{-1}$ g.-mol.$^{-1}$ l.) with a mean deviation of $\pm\,0{\cdot}50 \times 10^{-4}$ and a probable error of $\pm\,0{\cdot}15 \times 10^{-4}$. We consider the accuracy is good in view of the difficulties inherent in the radioactive measurements. Agreement with the more accurate constant for inversion ($k_I = 5{\cdot}24 \times 10^{-4} \pm 0{\cdot}05 \times 10^{-4}$ sec.$^{-1}$ g.-mol.$^{-1}$ l.) is within the experimental error, and the data amply justify the conclusion that in the system studied substitution leads to inversion.

## EXPERIMENTAL.

*Purification of Materials.*—Acetone was purified by careful fractionation from phosphoric oxide (cf. Spence and Wild, J., 1937, 352). Lithium bromide was recrystallised from acetone and dried.

*Preparation of* d-α-*Bromopropionic Acid.*—A commercial sample of lactic acid was converted into the methyl ester [$\alpha_D^{20°}$ ($l$ = 2) − 11·9°], hence into the bromo-ester [$\alpha_D^{20°}$ ($l$ = 1) + 31·8°], and finally into the bromo-acid [$\alpha_D^{20°}$ ($l$ = 1) + 20·7°] (cf. Cowdrey, Hughes, and Ingold, J., 1937, 1227). The rotation of the bromo-acid in acetone solution remained constant during the period of time required for complete racemisation by bromide ions under the conditions employed in the comparative experiments. Racemic bromo-acid for the exchange was a B.D.H. sample which was carefully fractionated.

*Racemisation.*—An acetone solution, N/3 with respect to each reactant, was prepared and introduced into a jacketed 2-dm. polarimeter tube maintained at 22·0°, and the fall in rotation followed in the usual way. The bimolecular velocity coefficients ($k_I$) were calculated from the expression given above. The results of a typical experiment are recorded in Table II.

TABLE II.

[*d*-α-Bromopropionic acid] = 0·334M.; [LiBr] = 0·314M.; Temp. = 22·0°; $t$ is the time in secs., α the rotation, and $k_I$ the bimolecular velocity coefficient in sec.$^{-1}$ g.-mol.$^{-1}$ l.

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $t$ | 0 | 342 | 678 | 942 | 1254 | 1548 | 1974 | 2316 | 2742 | 3222 | 3828 | 4458 | 5310 | 6900 |
| α | 1·60 | 1·40 | 1·26 | 1·15 | 1·02 | 0·91 | 0·79 | 0·70 | 0·60 | 0·51 | 0·42 | 0·33 | 0·23 | 0·13 |
| $10^4 k_I$ | — | 5·19 | 5·16 | 5·14 | 5·26 | 5·35 | 5·24 | 5·23 | 5·25 | 5·20 | 5·12 | 5·19 | 5·36 | 5·33 |

Average $k_I = 5{\cdot}23 \times 10^{-4}$.

*Exchange.*—A simple form of Geiger-Müller counter and recording circuit was used for measuring radioactivity. The ionisation chambers were made from aluminium tubing, as described in Part I (*loc. cit.*). The activity of lithium bromide was measured in solution (cf. Olson, Libby, Long, and Halford, *J. Amer. Chem. Soc.*, 1936, **58**, 1313), and for this purpose the window of the ionisation chambers was surrounded by a glass jacket fitted to the aluminium by rubber. The procedure adopted necessitated the comparison of activities of two samples; the chambers were therefore constructed in pairs as nearly identical as possible and placed so that they could alternately be switched to the counting circuit. The latter was a one-stage amplifier battery coupled to a thyratron and telephone counter (Fay and Paneth, J., 1936, 384). Each discharge chamber had its appropriate high-tension supply, and, although the response of each chamber to the same stimulus might differ by as much as 10%, their sensitivity ratio was determined by preliminary measurement and remained constant over long periods of use and greatly varying rates of counting.

Exchange was carried out under the conditions already given for racemisation. Lithium bromide was activated in acetone solution by a radium sulphate-beryllium neutron source.

The irradiated solution was divided into two parts: one portion was used for the exchange, the other was evaporated to dryness, the residue dissolved in 4N-sodium hydroxide, made slightly acid with 3N-nitric acid and the resulting solution placed around one of the ionisation chambers.

In the exchange, reaction was arrested after a given time by neutralising with 4N-sodium hydroxide. The acetone was evaporated in a vacuum, and 3N-nitric acid (1·5 equivs.) added. The solution was then extracted seven times with an equal volume of ether, under which conditions supplementary experiment had shown that at least 99% of the organic acid was extracted. The aqueous layer, containing the bromide, was placed around the second ionisation chamber. It is to be noted that both samples of lithium bromide were treated as far as possible in the same way.

Comparison of the activities of the two solutions of bromide ions was made by alternately switching each ionisation chamber to the counting circuit for a period of one minute. The minute counts were first corrected for coincidence by the usual quadratic formula and the background count was then subtracted. The figures obtained were summed for each sample over periods of an hour or more, and the sums further adjusted for the different sensitivities of the two chambers and the unequal concentrations of the two solutions of bromide ions. The latter were measured by Volhard titration after the radioactive measurements had been completed.

The final corrected ratio is given as $x/x_0$ in Table I.

We thank Professor C. K. Ingold for advice, and the Chemical Society for a grant.

The Sir William Ramsay and Ralph Forster Laboratories,
University College, London. [*Received, January 12th*, 1938.]

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## 40. *The Mesomeric Effect of the Sulphoxide Group.*

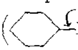
By D. Ll. Hammick and R. B. Williams.

The electric dipole moment of diisobutyl sulphoxide has been determined in benzene solution. Its value, 3·90 D., is less than that of diphenyl sulphoxide, 4·08 D., and hence the mesomeric effect of the sulphoxide group is negative. This should lead, on the electronic theory of benzenoid reactivity, to the expectation of attack by kationoid reagents in the *o*, *p*-positions in the benzene nucleus and by anionoid reagents in the *o*, *m*-positions. Owing to the fragility of the sulphoxide group, the first expectation could not be tested; the fact, however, that *p*-iododiphenyl sulphoxide is hydrolysed by alkali under conditions where the m-*iodo*-derivative is unaffected fulfils the second prediction.

It is shown that the charges on the sulphur, nitrogen, and iodine atoms in the sulphoxide, nitroso- and iodoxy-groups are positive; these groups are alike in respect to their inductive and mesomeric affects, which are negative and positive respectively.

The introduction of an atom or group X into the benzene molecule in place of a hydrogen atom produces a mesomeric effect *M* (Robinson, *J. Soc. Dyers Col.*, 1934, 65; Ingold,

*Chem. Reviews*, 1934, **15**, No. 2). The sign of *M* can be found from a comparison of the electric dipole moments of the corresponding alkyl and aromatic compounds with the substituent X (Sutton, *Proc. Roy. Soc.*, 1931, *A*, **133**, 668). Where data are not available for making this comparison, the sign of the mesomeric effect can be inferred from the orienting effect of X on further substitution in the benzene nucleus, because the Robinson theory of the orienting process requires *o*, *p*-reactivity towards kationoid reagents for a + *M* effect and *o*, *m*-reactivity for a − *M* effect.

Those atoms and groups which produce a + *M* effect fall into two classes. In the first, comparatively small, category, we find the alkyl groups and certain anionic centres such as $-\bar{O}$ (phenoxide ion), where the inductive and the mesomeric effect are both positive. In the second, we have atoms and groups in which, although the inductive effect is negative, the mesomeric effect is positive and dependent on covalency increase on the atom attached to the nucleus (  X, where X = $-NR_2$, –OR, halogens, etc.). This tendency for covalency increase to occur, with accession of electrons into the nucleus in spite of an opposing inductive effect, is so prevalent that special interest attaches to the few cases where the general rule is not obeyed. The first exceptional case was established for the nitroso-group, the electric dipole moment of nitrosobenzene being found to be greater than that of nitrosodimethylhexane by 0·63 D. (Hammick, New, and Sutton, J., 1932, 742). The existence of the –*M* effect, due presumably to a tendency to covalency decrease –N=O, was confirmed by the fact that *o*- and *p*-bromonitrosobenzenes are readily hydrolysed by aqueous silver nitrate (Hammick and Illingworth, J., 1930, 2358). *According to the Robinson theory of benzenoid reactivity, a –M effect will* facilitate attack by anionoid reagents ($NO_3^-$, $OH^-$) in the *o*- and *p*-positions.

The second exception is the iodoxy-group, $-IO_2$. Whatever the structure of this group may be, there must be at least two unshared electrons on the iodine atom. Nevertheless, nitration of iodoxybenzene (Masson, Race, and Pounder, J., 1935, 1669) *occurs in the m-position and hence the mesomeric effect must be negative.*

We have found in the sulphoxide group, >S–O, a third case of a substituent with unshared electrons on the atom next to a benzene nucleus exerting a negative mesomeric effect. We find that the dipole moment of diphenyl sulphoxide is greater than that of di*iso*butyl sulphoxide,* the negative sign of the mesomeric effect leading to the expectation of attack by kationoid reagents in the *m*,*o*-positions in the aromatic sulphoxide. It has not been possible to verify this prediction by direct experiment owing to the inability of the reactive sulphoxide group to withstand the drastic conditions necessary for *m*,*o*-substitution by kationoid reagents. We find, however, that *p*-iododiphenyl sulphoxide is hydrolysed by sodium hydroxide under conditions in which the m-*iodo*-derivative is unaffected.

## Experimental.

### *The Electric Dipole Moment of Diisobutyl Sulphoxide.*

The method and apparatus described by Sutton (*loc. cit.*) were used, benzene being the solvent.

*Preparation of Materials.—Diisobutyl sulphoxide.* This was prepared from di*iso*butyl sulphide, which was obtained from *iso*butyl alcohol by Beckmann's method (*J. pr. Chem.*, 1878, **17**, 445) with two modifications. First, a mixture of oleum and concentrated sulphuric acid was used instead of the latter alone for converting the *iso*butyl alcohol into the acid sulphate, for it was found that without the oleum much of the alcohol remained unchanged. Secondly, the crude di*iso*butyl sulphide was washed with concentrated potassium hydroxide solution in order to get rid of *iso*butyl mercaptan, formed as a by-product, and then with water, instead of only with water.

The sulphoxide was prepared from the sulphide by oxidation with nitric acid (Beckmann,

* This was chosen as the aliphatic sulphoxide most suitable for dipole-moment measurements, because it has a higher m. p. (68°) than most aliphatic sulphoxides and hence is more easily purified. It is, moreover, not hygroscopic as are many aliphatic sulphoxides.

*loc. cit.*), the crude product being purified by extraction with ligroin (b. p. 40—60°); m. p. 68·0° (Beckmann, *loc. cit.*, gives 68·5°).

*Benzene.* A. R. Benzene, thiophen-free, was purified, dried, and distilled according to Hampson, Farmer, and Sutton (*Proc. Roy. Soc.*, 1933, *A*, **143**, 147).

*Results.*—The results of the measurements, at 25° in benzene solution, are given in the table, where the symbols have their usual significance; the refractive indices relate to the mercury green line 5461. To minimise errors in the densities, the experimental values were plotted against $f_2$, the values used in the calculations and given in the table being obtained from the mean line.

| $f_2$. | $d$. | $\epsilon$. | $n^2$. | $P_2$. | $_{E}P_2$. |
|---|---|---|---|---|---|
| 0·00427 | 0·87415 | 2·36323 | 2·25604 | 359·01 | 48·70 |
| 0·00288 | 0·87404 | 2·33378 | 2·25632 | 360·91 | 48·37 |
| 0·00190 | 0·87397 | 2·31427 | 2·25672 | 361·50 | 49·48 |
| 0·00149 | 0·87394 | 2·30416 | 2·25675 | 360·59 | 48·71 |
| 0·00000 | 0·87382 | 2·2727 | 2·25712 | — | — |

At $f_2 = 0$, $P_2 = 364·0$ c.c. and $_{E}P_2 = 48·8$ c.c., whence $P_2 - {_{E}P_2} = 315·2$ c.c. and $\mu = 3·90$.*

*The Action of Hydroxyl Ions on* m- *and* p-*Iododiphenyl Sulphoxides.*

*Preparation of Materials.*—p-*Iododiphenyl sulphoxide.* The method of Willgerodt and Klinger (*J. pr. Chem.*, 1912, **85**, 308) was employed.

m-*Iododiphenyl sulphoxide.* This substance, not hitherto described, was prepared from m-*nitrodiphenyl sulphide* according to the scheme :

$$m\text{-}NO_2\cdot C_6H_4\cdot SPh \longrightarrow m\text{-}NH_2\cdot C_6H_4\cdot SPh \longrightarrow m\text{-}C_6H_4I\cdot SPh \longrightarrow m\text{-}C_6H_4I\cdot SOPh$$

Crude *m*-nitrodiphenyl sulphide, prepared from *m*-nitroaniline and sodium thiophenoxide according to the method described by Weedon and Doughty for *o*-methyldiphenyl sulphide (*Amer. Chem. J.*, 1905, **33**, 386), was steam-distilled for 65 hours, the distillate extracted twice with ether, and the combined extracts dried over calcium chloride. The brown oil left after removal of the ether solidified on cooling in a freezing-mixture and scratching. It was purified by extracting it twice with ligroin (b. p. 40—60°) at room temperature, about 80—90% being dissolved altogether, and cooling the extracts in a freezing-mixture in the presence of a seeding crystal. Vigorous scratching caused the *m*-nitrodiphenyl sulphide to separate as a pale yellow solid, which was filtered off, washed with ligroin (b. p. 40—60°), which had previously been cooled in a freezing-mixture, and dried in the air on a porous plate. Concentration and cooling of the mother-liquors yielded a further quantity of substance. 50·9 G. of *m*-nitroaniline and 43·3 g. of thiophenol gave 17·9 g. of this product. A further two extractions with ligroin of a portion of this product afforded the pure substance as pale yellow crystals, m. p. 42·5° (Found : S, 13·83; N, 5·88. $C_{12}H_9O_2NS$ requires S, 13·85; N, 6·06%).

8 G. of this sulphide were converted by reduction with stannous chloride and hydrochloric acid (cf. Mauthner, *Ber.*, 1906, **39**, 3593) into 5·7 g. (82% yield) of crude *m*-aminodiphenyl sulphide (an oil, solidifying in a freezing-mixture). This was converted by diazotisation and treatment with potassium iodide (cf. Willgerodt and Klinger, *loc. cit.*) into 3·7 g. of crude *m*-iododiphenyl sulphide (colourless oil). This was oxidised, with perhydrol in glacial acetic acid, to the sulphoxide (cf. Bergmann and Tschudnowsky, *Ber.*, 1932, **65**, 457). The crude product (3·4 g.; 88% yield) was purified by extraction with boiling ligroin (b. p. 60—80°) until about 90% had been dissolved. The solid separating on cooling in a freezing-mixture was recrystallised from 50% alcohol with norit, and finally from ligroin (b. p. 60—80°); colourless needles (1·6 g.), m. p. 73·5° (Found : S, 9·79. $C_{12}H_9OIS$ requires S, 9·76%).

*Hydrolysis of* p- *and* m-*Iododiphenyl Sulphoxide.*—Solutions of each of the isomers in equal concentration (0·3 g. in 30 c.c. of N/5-aqueous alcoholic potash, containing 60% alcohol by volume) were refluxed for 1 hour on the water-bath. After this treatment, the solution of the *p*-isomer was found to contain iodine ions, which were absent from the other solution.

## Discussion of Results.

The value obtained for the electric dipole moment of di*iso*butyl sulphoxide, 3·90, is numerically less than the moment of diphenyl sulphoxide, for which the following values

* All dipole moments in this paper are given in Debye units (e.s.u. × $10^{-18}$).

are available: 4·08 (Bergmann, Engel, and Sandor, *Z. physikal. Chem.*, 1930, *B*, **10**, 397), 4·17 (de Vries and Rodebush, *J. Amer. Chem. Soc.*, 1931, **53**, 2888), 3·99 (Hampson, Farmer, and Sutton, *loc. cit.*). That the sense of the dipole of the diphenyl sulphoxide molecule is as shown, $(C_6H_5)_2\overset{+\!\!\longrightarrow}{SO}$, follows from the fact that its value, 4·08, the mean of the three values quoted above, is greater than that, 2·57, of *pp'*-dichlorodiphenyl sulphoxide (Hampson, Farmer, and Sutton, *loc. cit.*). Hence the algebraic difference between the dipoles of the aliphatic and the aromatic sulphoxides is − 0·18, and this is a measure of the mesomeric effect of the sulphoxide group. A negative (outward) mesomeric effect means that the electromeric changes that occur on suitable activation will render the aromatic nuclei susceptible to attack by kationoid reagents in the *o*- and *p*-positions and by anionoid reagents in the *o*- and *m*-positions. The removal of iodine as ions from *p*-iododiphenyl sulphoxide by the action of hydroxyl ions, the *m*-isomer being unaffected, confirms this prediction.

The rule given by Sidgwick ("The Co-valent Link in Chemistry," pp. 180—181) may be put in a slightly more general form by saying that, whenever the atom attached to the benzene nucleus has a residual positive charge, the atom (or group to which it belongs) is *m,o*-orienting towards kationoid reagents; and it has been pointed out (Masson, Race, and Pounder, *loc. cit.*) that the orientation rule due to Hammick and Illingworth (*loc. cit.*) "is valid as to directive effect of groups XY only so far as it may correctly imply which elements, X, in the Periodic Classification are positive to which elements Y." It is therefore to be expected that the atoms by which the iodoxy-, nitroso-, and sulphoxide groups are attached to benzene nuclei should be positive with respect to the nuclear carbon.

For the case of the nitroso-group an approximate numerical calculation of the charge on the nitrogen atom can be made. The dipole moment of nitrosobenzene is 3·14 (Hammick, New, and Sutton, *loc. cit.*); the angle between the C–N and the N=O link is, however, not known. Most probably it lies between 125·25°, the normal angle between a single and a double bond for a tetrahedral atom, and 150°. Again, although the dipole moment in the Ph–N link is known to be directed towards the nitrogen atom, its value is in doubt but probably lies between 0·4 and 1·4. Of these values, 0·2 is contributed by the H–C link para to the nitroso-group, so that the C–N link probably has a moment between 0·2 and 1·2. The N=O link moment, which is directed away from the nitrogen atom, and the value of the residual charge on the nitrogen atom, depend on the values taken for the angle between the C–N and N=O links and for the Ph–N moment. These data, in conjunction with the interatomic distances 1·48 and 1·21 A. for the C–N and the N=O link (these and other link lengths are computed from Sidgwick's values for atomic radii, *op. cit.*, p. 83) yield maximum and minimum values for the charge on the nitrogen atom of + 0·48**e** and + 0·15**e**.

In the case of the sulphoxide group a similar calculation yields a positive value for the charge on the sulphur atom; the dipole model is, however, too crude to be used with any confidence to make even approximate computations. We therefore make the reasonable inference that the separation of charge associated with the co-ordinate link will establish a positive charge on the sulphur atom due to the $S \rightarrow O$ link greater than any positive charge on the nuclear carbon atom that could result from separation of charge in the covalent C–S links.

Very similar considerations apply to the iodoxy-group. There can be little doubt but that the two iodine–oxygen links leave a positive charge on the iodine atom greater than the negative charge it receives as a result of its linkage to a carbon atom in the nucleus.

It thus appears that there are two classes of substituent which exert a negative (outward) inductive effect on a benzene nucleus. In the first class we have groups and atoms such as $-NH_2$, $-OR$, and the halogens, where the charge on the carbon atom in the nucleus is positive with respect to the atom next to it ($\gg\overset{\delta+}{C}—\overset{\delta-}{\overset{\delta-\,\delta+}{NH_2}}$, $\gg\overset{\delta+}{C}—\overset{\delta-}{Cl}$, $\gg\overset{\delta+}{C}—\overset{\delta-}{\overset{\delta-}{O}}—\overset{\delta+}{H}$). The second class contains the groups NO, $IO_2$, and SO, in which there is a positive charge on the nuclear carbon atom due to separation of charge in the links $\gg\overset{\delta+}{C}—\overset{\delta-}{N}$, $\gg\overset{\delta+}{C}—\overset{\delta-}{I}$ and

$\geqslant\overset{\delta+}{C}-\overset{\delta-}{\overset{\delta-}{S}}-\overset{\delta+}{C}\leqslant$ and + charges also on the nitrogen, iodine, and sulphur atoms due to the polarisation of the links $\overset{\delta+}{N}=\overset{\delta-}{O}$, $\overset{\delta+}{I}=\overset{\delta-}{O_2}$ and $\overset{\delta+}{S}-\overset{\delta-}{O}$; thus $\geqslant\overset{\delta+}{C}-\overset{\delta-}{\overset{\delta+}{N}}=\overset{\delta-}{O}$, $\geqslant\overset{\delta+}{C}-\overset{\delta-}{\overset{\delta+}{I}}=\overset{\delta-}{O}$ and $\geqslant\overset{\delta+}{C}-\underset{\overset{\downarrow}{O_{\delta-}}}{\overset{\delta-}{\overset{\delta-}{\overset{\delta+}{S}}}}-\overset{\delta+}{C}\leqslant$. But only the first group appears to be able to contribute electrons to electromeric processes leading to *o*, *p*-activation towards kationoid reagents; the groups in the second class do not do this, and it appears reasonable to connect this fact with the presence of a net positive charge on the atom next to the nucleus.

Our thanks are due to Dr. L. E. Sutton for permission to use his apparatus and to him and Dr. G. C. Hampson for helpful advice. We also gratefully acknowledge a maintenance grant from the Department of Scientific and Industrial Research (to R. B. W.) and a grant from Imperial Chemical Industries, Ltd.

The Dyson Perrins Laboratory, Oxford. [*Received, December 2nd*, 1937.]

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## 41. *The Chemistry of Natural Rubber.* Part I. The Isolation of the Constituents.*

By Kenneth C. Roberts.

Finality of outlook has not yet been reached on many aspects of rubber science. Opposing views are held on the most fundamental phenomena, such as the elasticity of rubber and its behaviour on exposure to air and light, and even its elementary composition and its molecular weight are still subjects of discussion. Until now no single comprehensive process has existed for the separation of natural rubber into its constituents, and it was felt that the development of such a process might throw light on some at least of the debated points.

The material hitherto regarded as the rubber hydrocarbon consists of two constituents—caoutchene and caoutchol (see following paper)—each of which lacks certain fundamental properties of natural rubber. Other points established are (*a*) the existence of two new minor non-hydrocarbon constituents, (*b*) the separation of the phosphatic material into two contrasted fractions, and (*c*) the failure to separate completely the major nitrogenous constituent and the rubber hydrocarbon.

Quantitative analyses based on the process are proving of value in approaching the problems of the variability of latex and of rubber, the effect of preservation on latex, and latex metabolism.

It is generally accepted that the solid matter which constitutes 30—50% of the latex of *Hevea brasiliensis* (the source of almost the whole of the raw rubber of commerce) consists essentially of the rubber hydrocarbon ($\sim$ 90%) together with small and varying amounts of mineral phosphates, sugars, quebrachitol (*l*-methylinositol), fatty acids, sterols, and nitrogenous matter including protein. Raw rubber and the various concentrated latices of commerce contain all these constituents, but owing to their modes of preparation they contain in general a more or less reduced amount of water-soluble matter, *viz.*, phosphates, sugars, quebrachitol, and nitrogenous matter.

Many detailed investigations of individual constituents have been reported, but there is in general use for the examination of latex or of rubber no method which involves the isolation of the constituents in the forms in which they occur in the raw product. In this respect no advance has been made on the work of Faraday, who (*Quart. J. Sci.*, 1826,

* A brief account of preliminary work on this subject has already been published (Roberts, *J. Rub. Res. Inst. Malaya*, 1936, 7, 46).

**21**, 19) reported the quantitative isolation of the constituents of a rubber-bearing latex from Mexico.

Present practice is to indicate the composition of rubber in terms of its content of "resin" (acetone extract), "sugars" (reducing power of water extract), ash, "protein" (nitrogen content × 6·25), and "hydrocarbon" (the elastic residue). This has led to preconceptions on the part of many workers in this field. The nature of the substances responsible for the reducing power of the water extract of rubber is not yet well established, and attempts to isolate a protein have met with only partial success. Further, the current view that the essential rubber "substance"—the above elastic residue—is a hydrocarbon, is not well founded. The precise analytical data of Midgley, Henne, Shepard, and Renoll (*J. Amer. Chem. Soc.*, 1935, **57**, 2318) have shown that the elastic constituent of rubber contains a small but definite amount of hydroxylic oxygen.

In developing the present method for the isolation of the constituents, a departure has been made from current practice. Whereas it is customary to remove non-hydrocarbon material from rubber by extraction processes, the primary separation is now effected by treating a solution of rubber in such a way that the purely organic non-hydrocarbon constituents are retained in solution on removal of the hydrocarbon and the mineral-containing constituents by precipitation. To this end, the rubber is dispersed in an approved mixture of carbon tetrachloride and acetone, and the dispersion is treated with a further quantity of acetone (see scheme).

There is a two-fold reason for the use of the mixed dispersing agent: first, it expedites the notoriously slow process of dispersion of rubber by taking advantage of the fact that addition of acetone to such dispersions markedly reduces their viscosity; secondly, it exploits a possibility which does not appear to have been appreciated hitherto, that this reduction of viscosity may be due to a breakdown of the micellar structure of dispersed rubber in presence of acetone. If such a breakdown takes place, the rubber in the mixed dispersing agent will approach more closely to a true unimolecular state than in a simple solvent.

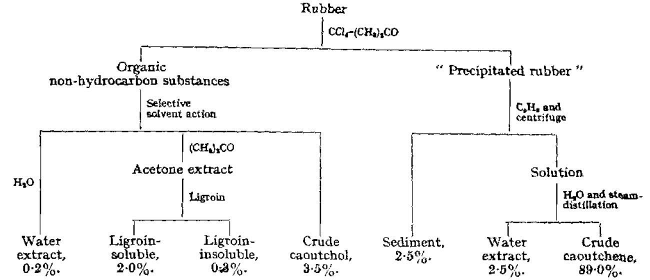
The principle employed in the further treatment of both the organic non-hydrocarbon material and the "precipitated rubber" (the mixture of hydrocarbon and mineral-containing constituents will be thus referred to) is to submit each to treatment by physical, as opposed to chemical, means until the ultimate constituents of the raw material are obtained.

For this purpose the organic non-hydrocarbon material is treated by selective solvent action (see scheme). First, by means of water, a small amount of a hitherto undetected organic material containing nitrogen is removed. The acetone-soluble portion of the remainder is further separable into ligroin-soluble and ligroin-insoluble portions. Preliminary work shows that the former consists essentially of a group of substances hitherto isolated from the "acetone extract" of rubber, which has been examined in some detail by Bruson, Sebrell, and Vogt (*Ind. Eng. Chem.*, 1927, **19**, 1187) and by Whitby, Dolid, and Yorston (J., **1926**, 1448). The ligroin-insoluble material, on the other hand, has not previously been detected. The portion of the organic non-hydrocarbon matter remaining after these extractions has novel characteristics. It is an elastic substance which comprises 2—5% of the solid matter of raw rubber, but differs from rubber in that it readily dissolves in ether to give clear solutions having a very low viscosity. For reasons which appear in the ensuing paper, this new substance has been named "crude caoutchol."

The above non-hydrocarbon constituents all burn without ash. Further, they contain only very small amounts of nitrogen and quebrachitol and give no evidence of the presence of the free reducing sugars frequently stated to be present in rubber. The inference is that practically the whole of the quebrachitol, mineral and nitrogenous matter, and sugars of the original rubber is retained by the "precipitated rubber."

The effect of the removal of the new constituent caoutchol is immediately seen in the properties of the "precipitated rubber," which is characterised by its lack of tensile strength and by the remarkably low viscosity of its solutions in the usual rubber solvents. These properties have been utilised for the removal of further non-hydrocarbon materials

(see scheme). Thus the viscosity of a 3—4% solution of the "precipitated rubber" in benzene is sufficiently low for undissolved non-hydrocarbon material to be removed from




Scheme illustrating the separation of the constituents of *Hevea* rubber.

The constituents occupying the lowest line appear to be the ultimate ones separable by usual physical processes. The figures represent typical amounts of each, and are expressed as percentages of the total solid matter of latex.

it by centrifugal action. Further, the non-hydrocarbon material retained by the mobile solution after this treatment may be quantitatively removed in water by the procedure described below. The sediment and the water-extractable material so obtained together comprise the substances hitherto known as the "serum solids" of latex or as the water-soluble matter of rubber, but this is the first occasion on which a separation of this matter into two well-defined fractions has been effected.

The non-hygroscopic, water-soluble sediment and the hygroscopic water extract together contain only about one-fourth of the total nitrogen of rubber (unpublished results), the major portion of which therefore remains associated with the residual rubber. The point is now emphasised that all attempts to separate the latter quantitatively into a nitrogenous constituent and a pure hydrocarbon have completely failed. The nature of the retained nitrogenous matter remains obscure. It is proposed to call the nitrogen-containing residue "crude caoutchene," and to reserve the name "caoutchene" for the pure hydrocarbon. Crude caoutchene is remarkable in that it is notably deficient in toughness and elasticity, properties hitherto regarded as fundamental attributes of the essential rubber substance.

With a view to determining the effect of a variety of factors on the composition of latex and of rubber, the separation of rubber into the above seven constituents has been placed on a quantitative basis. The table summarises the results of typical analyses of the total solid matter of latex and of a high-grade crêpe rubber.

| Components of primary separation. | Constituent. | Item No. | Per cent. of total solids. I, Latex. | II, Crêpe. |
|---|---|---|---|---|
| Organic non-hydrocarbon material | Water extract | 1 | 0·28 | 0·03 |
| | Acetone extract: (i) Ligroin-insol. | 2 | 0·27 | 0·14 |
| | (ii) Ligroin-sol. | 3 | 2·37 | 1·75 |
| | Crude caoutchol | 4 | 4·71 | 3·23 |
| "Precipitated rubber" | Sediment | 5 | 2·75 | 0·01 |
| | Water extract | 6 | 2·12 | 0·24 |
| | Crude caoutchene | 7 | 87·02 | 94·04 |
| | Total | — | 99·52 | 99·44 |

The newly discovered material caoutchol is seen to be the major non-hydrocarbon constituent of rubber.

The percentage of non-hydrocarbon matter for the above typical specimen of *Hevea* latex (col. I) is higher than that usually reported in spite of the absence of the usual item

"protein," which is now included under crude caoutchene. Comparison of cols. I and II shows that the water-soluble matter (items 1, 5, and 6) is largely removed in the preparation of crêpe rubber. The differences between the other pairs of figures are not unusual for a biological fluid.

## Experimental.

The finely divided, dried sample of rubber (30 g.) is added to a mixture of carbon tetrachloride (700 c.c.) and acetone (450 c.c.). The mixture is stirred intermittently until a homogeneous, opalescent and relatively mobile dispersion results, usually in 2—4 hours, but the mixture is kept in subdued light for 24 hours to allow time for the break-down of the micellar structure. A further 450 c.c. of acetone are then added while the mixture is agitated. The crude caoutchene together with phosphatic matter is quantitatively precipitated in fine white flakes, which slowly coalesce. After the mixture has been kept for 24 hours in subdued light, the supernatant, clear, pale yellow solution is decanted, and the "precipitated rubber" is washed first with 50 c.c. of a mixture of carbon tetrachloride (7 vols.) and acetone (9 vols.) and finally with acetone (50 c.c.). The combined solution and washings are distilled to small bulk and the remaining solvent is removed on a water-bath. The residue consists of the organic non-hydrocarbon constituents.

*Treatment of the Organic Non-hydrocarbon Constituents.—Water extraction.* The oily, dark-coloured material is extracted three or four times with small quantities of water, and the resulting pale yellow, slightly opalescent extract is dried on the water-bath. The product (approximately 0·2% of the total solid matter of latex) frequently includes as impurity a small amount of quebrachitol, which may be removed by treating the product with ethyl alcohol, in which quebrachitol is insoluble. The purified material is a viscous yellow oil which slowly deposits crystals.

*Acetone extraction.* The material remaining after the water extraction is stirred vigorously several times with warm acetone until all acetone-soluble material has been dissolved. Acetone is removed from the extract on the water-bath and the residue is resolved with ligroin.

The ligroin solution, dried to constant weight, yields a very viscous, dark red oil (1·5—2·5% of the rubber), which comprises the bulk of the acetone-soluble material. It slowly deposits crystals, and preliminary investigation of its hydrolytic products shows it to consist essentially of a complex of aliphatic acids, complex alcoholic substances, and a glucoside, together with small amounts of unidentified terpenic material. A small amount of a water-soluble, odorous, sulphur-containing substance is also present.

The ligroin-insoluble matter, constituting approximately 0·3% of the rubber, appears to consist of unsaturated higher aliphatic acids combined with an unidentified water-soluble substance.

The acetone-insoluble residue, dried on the water-bath, varies somewhat in texture from sample to sample, but is in general a transparent, brown, plastic solid possessing a high degree of elasticity and constituting 2—5% of rubber. It contains a small amount of sulphur. It dissolves rapidly in rubber solvents and in ether, giving very mobile and almost clear solutions, but is insoluble in alcohol. It is a crude form of the substance caoutchol described in the ensuing paper.

*Treatment of the "Precipitated Rubber."*—The washed "precipitated rubber" (cf. above) is rolled to a thin sheet on a mill and allowed to dry by evaporation in subdued light at room temperature (24 hours). A solution of the material (10 g.) in benzene (300 c.c.) is kept in a centrifuge for 30 minutes at 2000 r.p.m., and the supernatant, clear yellow solution is then decanted. The sediment, representing approximately 2·5% of the total solid matter of latex, is carefully washed with small quantities of benzene and may be weighed. It is a white, non-hygroscopic powder which is essentially soluble in water, although it is liable to be contaminated with traces of rubber and also with any fine dirt (earth, bark scrap, etc.) which was present in the original specimen. Latex is as a matter of routine purified by sieving, but the nature of the liquid permits of the removal only of coarser impurities by this method.

The benzene solution, together with the washings, is treated with water (1000 c.c.) in a 2-l. flask. The mixture, shaken to an emulsion, is distilled with steam. A clear liquid and a spongy white mass remain in the flask. After decantation of the liquid, the residue is rinsed several times with water, and the liquid expressible from it is added to the main bulk, which, after being concentrated on a hot-plate, is finally dried to constant weight on the water-bath. The pleasantly odorous, clear brown, vitreous product, representing approximately 2·5% of

the total solid matter of latex, is highly hygroscopic and forms large crystalline plates in contact with moist air.

The washed spongy mass is passed through a rolling mill before being dried in a vacuum over sulphuric acid. The tacky, very feebly elastic product retains the bulk of the nitrogen of the original material [Found: N (original rubber), 0·55%; N (residue), 0·42%]. It constitutes about 89% of the total solid matter of latex. A description of the material, which is named crude caoutchene, and an account of unavailing attempts to remove further non-hydrocarbon matter from it will be found in the ensuing paper.

*Notes.*—(1) Benzene may take the place of carbon tetrachloride in the initial stage of the process, but the acetone, owing to its highly specific action, is not replaceable by other common precipitants for rubber, such as alcohol. When benzene is used, the above proportions of solvent and precipitant require modification.

(2) The process has been carefully examined, particularly with respect to the possibility of oxidative or other changes in the constituents. No evidence of such changes has been obtained.

(3) The process lends itself to the analysis of any of the forms of raw rubber commonly met with, *viz.*, crêpe, smoked sheet, crumb, powder, or liquid latex. The last is conveniently prepared for analysis by spreading it in a thin film on plate-glass and drying it at 50—55° in a dark chamber. Analyses of latices and rubbers, the preparation of which has involved special chemical or other treatment, naturally present additional features. These will be reported elsewhere.

(4) Carbon tetrachloride is readily recoverable from the process by treating the distilled carbon tetrachloride-acetone mixture twice with large volumes of water.

Rubber Research Institute of Malaya,
Kuala Lumpur, Federated Malay States. [*Received, November 23rd, 1937.*]

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## 42. *The Chemistry of Natural Rubber. Part II. Caoutchene and Caoutchol and the Intermolecular Structure of Rubber.*

By Kenneth C. Roberts.

The two components of the material hitherto regarded as the rubber "substance" (cf. preceding paper) are described.

Crude caoutchene, the major component, comprises 95—98% of this material, and consists essentially of a typical polyterpene, caoutchene. It is tacky and only feebly elastic. With it is very intimately associated a small amount of unidentified nitrogenous matter. Molecular-weight evidence indicates that *caoutchene* is an octaterpene, $C_{80}H_{128}$, the molecules of which are considerably associated at room temperature.

Crude caoutchol, constituting 2—5% of the former rubber "substance," consists of an alcohol, *caoutchol* (~ 97%), in combination with complex unidentified acidic material (2—3%) which contains sulphur. The evidence suggests that caoutchol is a dihydrate, $C_{80}H_{130}(OH)_2$, of caoutchene. The alcohol freshly purified by hydrolysis is a tough non-tacky substance which resembles rubber in being highly elastic, but differs from it in dissolving freely in ether to clear mobile solutions. The molecules of the freshly prepared substance are appreciably associated at room temperature.

The influence of caoutchol on the physical properties of plantation rubber is discussed. Evidence from viscosity measurements and other considerations in support of a two-phase intermolecular theory is adduced.

Two views of the nature of purified rubber are widely current—one, that it is composed of very large, open-chain hydrocarbon molecules having a molecular weight of the order of 100,000 (Staudinger and collaborators, 1920—1937. For a summary, see Staudinger, *Trans. Inst. Rub. Ind.*, 1934, **10**, 263); the other, that it consists of micellar aggregates of relatively small hydrocarbon molecules having a molecular weight of 1100—1600 (Pummerer, *Ber.*, 1927, **60**, 2167; 1928, **61**, 1591; 1929, **62**, 2628). The first is based primarily on consideration of the viscosity of rubber solutions, and the second on cryoscopic molecular-weight determinations of rubber in camphor and similar solvents.

Neither view provides a basis for a convincing explanation of the remarkable degree of elasticity of raw rubber. Midgley, Henne, Shepard, and Renoll (*J. Amer. Chem. Soc.*, 1935, **57**, 2318) on the basis of analytical evidence have advanced the further view that the rubber molecule contains a hydroxyl group and has a minimum molecular weight of 40,000.

New light is thrown on the subject by the separation of the supposed rubber "substance" into two constituents (see preceding paper), crude caoutchene and crude caoutchol (95—98% and 5—2% respectively of the former rubber "substance").

*Caoutchene.*—Crude caoutchene, the tacky, feebly elastic material which constitutes 87—91% of the total solid matter of *Hevea* latex, consists preponderantly of carbon and hydrogen (~ 99%) together with small amounts of nitrogen, sulphur, and oxygen (~ 1%). Attempts to remove nitrogenous matter have proved unavailing. Midgley, Henne, and Renoll (*J. Amer. Chem. Soc.*, 1931, **53**, 2733) have, however, isolated from rubber by fractional precipitation at the critical temperature a small amount of nitrogen-free material, and it is therefore inadmissible to conclude that nitrogen is a component of the rubber molecule. It is accordingly assumed that crude caoutchene consists of a hydrocarbon in intimate association with an unidentified nitrogenous constituent. Analytical and molecular-weight evidence indicates that the hydrocarbon is an octaterpene, $C_{80}H_{128}$, to be called *caoutchene.* It is noteworthy that the nitrogen content of crude caoutchene from numerous specimens of fresh latex has remained practically constant ($0{\cdot}42 \pm 0{\cdot}05\%$) over a period of months. The nitrogen content of crude caoutchene from other sources is discussed in the experimental section. Two points have been established concerning the nature of this nitrogenous matter: (1) the nitrogen is, at least in part, of amide type; (2) the relative amounts of nitrogen, oxygen, and sulphur are similar to those found in typical proteins.

Crude caoutchene is not a pure substance, but it may readily be shown that, since the amount of nitrogenous constituent present is very small, variation of its carbon/hydrogen ratio within quite wide limits will not cause a material divergence of the carbon/hydrogen ratio found for *crude* caoutchene from that of *pure* caoutchene. Any divergence will be inappreciable if the nitrogenous constituent is protein, the average carbon/hydrogen ratio for which (10/15·7) is very close to that of the terpenes (10/16). In other words, the carbon and hydrogen values found for crude caoutchene may fairly be taken as representing those of the hydrocarbon constituent. Thus from typical findings of C, 87·1; H, 11·8% for crude caoutchene, C, 88·1; H, 11·9% may be calculated for the hydrocarbon constituent, figures which are in good agreement with those required for $(C_5H_8)_x$, *viz.*, C, 88·2; H, 11·8%. In this connection attention is drawn to the remarkably close physical resemblance between caoutchene as now obtained and the synthetic polyterpene, polymyrcene, of undetermined molecular weight, which is also a tacky mass (Harries, *Ber.*, 1902, **35**, 3264).

The molecular weight of crude caoutchene in melting camphor lies between 990 and 1170 ($C_{80}H_{128}$ requires 1088). Objections to the Rast method on the grounds that the high temperature involves decomposition of the rubber have been refuted elsewhere (Pummerer, Andriessen, and Gündel, *Ber.*, 1929, **62**, 2628), but it may also be mentioned that repeated cooling and remelting of a camphor solution of crude caoutchene produces no change in the melting point. Further, the molecular weight now observed is much lower than that of 3400 reported by Staudinger and Bondy (*Annalen*, 1929, **468**, 1) for rubber heated in solution at a considerably higher temperature, *viz.*, 206°. Crude caoutchene undoubtedly exists in a considerably associated state at room temperature. The viscosity of its solutions, though of a different order from that of identical solutions of raw rubber (see Table, p. 221), is nevertheless considerable, and it has proved impossible to determine its molecular weight in benzene. Carothers and collaborators have shown (*J. Amer. Chem. Soc.*, 1930, **52**, 5279) that the intermolecular cohesive forces in paraffin hydrocarbons having a molecular weight of about 1000 approach the strength of the intramolecular C–C link. It is therefore to be expected that caoutchene should exist in a very strongly associated state.

*Caoutchol.*—Crude caoutchol is composed of an alcohol *caoutchol* (97—98%) in

combination with a small amount of a complex mixture of unidentified aliphatic acids (2—3%). In view of the experimental evidence, and because of the close relationship of caoutchol to caoutchene, the alcohol is considered to be the octaterpene dihydrate $C_{80}H_{130}(OH)_2$. It is nitrogen-free, but contains in addition to the above acids a variable and very small amount of an acidic sulphur-containing substance which has not yet been identified. Pure caoutchol prepared by hydrolysis of the crude product exists in the unimolecular form in melting camphor. Viscosity and benzene freezing-point observations indicate a considerable degree of association of its molecules in solution at room temperature.

Caoutchol contains 2·8% by weight of oxygen. Raw rubber, containing 2—5% of caoutchol, may therefore, after being freed from its other non-hydrocarbon constituents, contain as little as 0·05% of oxygen. This figure is in excellent agreement with that of 0·04—0·05% arrived at by Midgley, Henne, Shepard, and Renoll (*loc. cit.*) from a consideration of the results of analyses of rubber itself. This amount is so small as to evade detection by ordinary analytical technique. In any case, the prevailing belief that the rubber hydrocarbon is readily oxidised under atmospheric conditions has led the majority of investigators to regard oxygen found in purified rubber as having been adventitiously acquired.

The basis of the view of the physical nature of rubber now to be discussed is the remarkable degree of elasticity displayed by caoutchol, which, when freshly prepared, is as highly extensible as raw rubber itself. In view of its relatively low molecular weight (1124), this phenomenon must apparently be attributed to association of the molecules of the substance by means of their hydroxyl groups. A substance composed of long molecules associated in this way would inevitably form a complex network which might be expected to show the observed characteristics. It has been mentioned above that caoutchene, the major constituent of rubber, is relatively feebly elastic, exhibiting rather the highly viscous nature to be anticipated in a polyterpene. It is therefore suggested that the elasticity of raw rubber is essentially that of the minor constituent caoutchol, which in virtue of its own state of association and of its power of forming further associated links between its hydroxyl groups and the residual affinity of the caoutchene molecules, acts as a binding material which imparts its own elasticity to the entire mass.

A two-phase theory of the nature of rubber, similar in outline to the above, has been put forward by Fessenden (*J. Franklin Inst.*, 1896, **142**, 187; cf. Whitby, "Plantation Rubber and the Testing of Rubber," p. 257) from theoretical considerations, and a similar view of the structure of muscle has been advanced by Meyer and Picken (*Proc. Roy. Soc.*, 1937, *B*, **124**, 29).

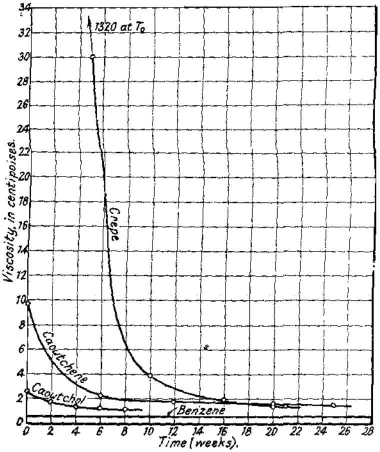
The elasticity of certain synthetic rubber substitutes may not be explained on the above basis, and is presumably due to the enormously high degree of polymerisation of their thread-like molecules. These would, by becoming entangled, impart to the material a matted structure which would resist deformation.

The two-phase intermolecular theory receives strong support from the following considerations. The viscosity measurements of contrasted specimens of rubber in freshly prepared solutions at the same concentration fall into two groups, one having viscosities of at least 1000 centipoises, the other of at most 100 centipoises (Table).

| Specimen. | Viscosity of 3·8% soln. in benzene. |
|---|---|
| Latex total solids | 6300 centipoises |
| ,, ,, ,, acetone-extracted | 4100 ,, |
| Pale crêpe rubber | 1320 ,, |
| Pale crêpe acetone-extracted | 1040 ,, |
| "Precipitated rubber" (cf. Part I) | 15—100 ,, |
| Crude caoutchene | 10—30 ,, |
| Caoutchol | 2—4 ,, |

All the specimens which contain caoutchol are in the former group, and the latter consists of those from which caoutchol has been removed. The low figure for caoutchol is noteworthy.

Further, the initial very high viscosity of a solution of crêpe rubber when kept in a closed vessel in diffuse daylight rapidly approaches a low value similar to that reached by caoutchol-free rubber solutions and by caoutchol solutions under the same conditions (Figure). When kept in the dark, however, solutions of raw rubber retain their intermolecular structure: during 20 weeks, the viscosity of a 3·8% benzene solution of crêpe rubber fell only from 1320 to 920 centipoises. Staudinger considers (*Trans. Inst. Rubber Ind.*, 1934, **10**, 276) that the fall in viscosity in light is due to disruption of the rubber molecule by traces of atmospheric oxygen, but because of the magnitude of the effect now recorded and of the cryoscopic evidence discussed above, the writer prefers to regard it as due to a lowering of the degree of association. Further, crêpe rubber contains the naturally occurring non-hydrocarbon constituents which are well known to protect the hydrocarbon from oxidation. Evidence in favour of the disaggregation of rubber




*Changes of Viscosity of 3·8% Solutions in Benzene of Crêpe Rubber, Caoutchene and Caoutchol in Diffuse Daylight.*

without oxidation has been advanced by others (for a summary, see Fisher, *Chem. Reviews*, 1930, **7**, 70). Additional support for this view is provided by the observation that crude caoutchene may be liquefied under conditions which preclude either oxidation or dissociation of its molecule (see Experimental).

The vital rôle of caoutchol in imparting elasticity to plantation rubber is further indicated by the parallel behaviour of caoutchol and of rubber under the action of heat. Caoutchol, which is tough at room temperature, is soft and plastic at 50—60° and is a viscous fluid at 100°. Correspondingly, rubber, which retains considerable elasticity at 45°, is preponderantly plastic at 70° (Hauser, Rosbaud, and Schmidt, *Kautschuk*, 1928, **4**, 12; Memmler, "Handbuch der Kautschukwissenschaft," p. 655). Further, the *X*-ray diffraction pattern produced by stretched rubber in virtue of its elasticity vanishes under diverse conditions between 40° and 90° (von Susich, *Naturwiss.*, 1930, **18**, 915; Pummerer and von Susich, *Kautschuk*, 1931, **7**, 117). It is suggested that this temperature range is determined by the fact that caoutchol loses its elasticity within the same range. The diffraction of *X*-rays by caoutchene and caoutchol is now being investigated in this laboratory.

The action of caoutchol on caoutchene is apparently highly specific, but other substances also have a marked effect on the physical nature of caoutchene. Thus the "precipitated rubber" (preceding paper), which consists of crude caoutchene together with the bulk of the water-soluble matter of latex or rubber, though it resembles crude caoutchene in being readily soluble and only slightly elastic, is tougher and less self-adhesive. It has also been observed that a film consisting of the total solid matter of latex is mechanically much stronger than raw plantation rubber, from which practically all water-soluble matter has been removed. Crude caoutchene in the wet state is also tough and non-tacky. The presence of certain non-elastic materials therefore appears to impart toughness to caoutchene, without, however, appreciably increasing its elasticity. One may compare the analogous action of small amounts of divinylbenzene in changing the character of polystyrene (Staudinger, *Ber.*, 1935, **68**, 1618).

The highly specific rôle of acetone in permitting the separation of caoutchol and caoutchene may be explained on the above view of the nature of rubber. It is suggested that the presence of a certain limited amount of acetone in a rubber dispersion causes a redistribution of co-ordinate links, links between the carbonyl-oxygen of acetone and the hydroxyl group of caoutchol being formed preferentially to those between molecules of caoutchol and caoutchene which normally persist in a dispersion. In this way the usual intermolecular structure of a dispersion is destroyed and the viscosity undergoes the observed reduction. In other words, the caoutchol is in a sense "solvated" by the acetone, and it ceases to maintain the intermolecular structure of the dispersed rubber, which is thus free to dissolve. Carefully regulated addition of more acetone quantitatively precipitates caoutchene (and the attendant insoluble inorganic matter) while the "solvated" caoutchol remains dissolved. In this way the resolution of the essential rubber "substance," which has so long eluded investigators, is effected. Still further addition of acetone will reduce the concentration of carbon tetrachloride (or other rubber-dispersing medium) to the point at which it can no longer hold caoutchol in solution, and the caoutchol, somewhat more soluble than caoutchene, will then be precipitated.

## EXPERIMENTAL.

*Crude Caoutchene*.—Several of the physical characteristics of the material described by this name in the preceding paper have been mentioned in the foregoing. The material varies considerably in texture according to the previous history of the specimen, that obtained from fresh latex being more tacky (less highly associated) than that from plantation rubber. Additional data are: (*a*) Crude caoutchene has no definite melting point. When maintained at 100° under reduced pressure for 1—2 hours, it changes to a pale brown highly viscous liquid without increase in weight. When heated at 100° in air, it slowly oxidises (Found: Increase in weight after 24 and 48 hours at 100° in air, 0·32 and 3·30% respectively). This reaction will be discussed more fully in a later communication. (*b*) It is extensible without rupture by only 100—200% and shows very poor elastic recovery. It has proved impracticable (see next paragraph) to purify the material further, and it has therefore been brought to analysis in the crude state [Found, *e.g.*: C, 87·0; H, 11·8; N, 0·5; S, 0·1; O (by diff.), 0·6; *M* (Rast), 1050, 1109 ± 60. Whence may be deduced for pure caoutchene (cf. discussion above): C, 88·0; H, 11·9%. $(C_5H_8)_{16}$ requires C, 88·2; H, 11·8%; *M*, 1088]. Within the limits of error of the determinations, the oxygen content is equivalent to the nitrogen content. The analysis is typical of those obtained for crude caoutchene from fresh latex and from plantation rubber.

*The Nitrogenous Constituent*.—It has been mentioned above that a quantitative separation of caoutchene and the major portion of the nitrogenous matter of rubber has not been effected. This is the more remarkable in that crude caoutchene dissolves readily and almost without swelling in the usual rubber solvents and in ether to give solutions which are remarkably mobile and in some cases water-clear. The ethereal solution is opalescent, but prolonged centrifuging of both the ethereal and the benzene solution failed to remove any undissolved matter. Solutions of crude caoutchene were kept for 6 months in diffuse daylight, until their viscosity approached that of the solvent itself (Figure). Such solutions gave no evidence of the separation of insoluble matter (Found for dissolved matter: N, before exposure, 0·4; after 6 months' exposure, 0·4%). A further unsuccessful attempt to remove nitrogenous

matter from crude caoutchene involved prolonged continuous extraction of a benzene solution with 90% formic acid (Found for extracted caoutchene: N, 0·38%). It has been shown by Wilkins (*Science*, 1937, **85**, 526) that this reagent quantitatively removes the protein from dried grasses. Low values for the nitrogen content of crude caoutchene have been observed only for specimens prepared from the dried solids of creamed latices (Found: N, 0·3, 0·1, 0·3, 0·1, 0·1, 0·2% for the products of various processes). The creaming of latex involves a partial separation of the larger and the smaller globules, the latter tending to remain in the serum. The above results therefore indicate that the smaller latex globules contain a higher concentration of the nitrogenous constituent than the larger. Other "low-nitrogen rubbers" of commerce do not come into consideration in this connection, since they are prepared by treatments designed to remove nitrogen chemically.

*Caoutchol.*—Crude caoutchol (10 g.), isolated from the organic non-hydrocarbon matter of rubber as described in the preceding paper, is heated under reflux for 1 hour with 1% aqueous caustic soda (200 c.c.). The cooled product is filtered off (a coarse, hardened paper is advisable), and the residue washed with water on the filter.

(*a*) The residue. For complete removal of alkali, the product should be repeatedly passed through the closed rolls of a mill fitted with a water spray. It is thus obtained as a thin, elastic, opaque sheet which may be dried in a vacuum over sulphuric acid in 24 hours. The resulting substance, *caoutchol*, is transparent, pale brown, and non-self-adhesive, and is extensible by at least 700% with immediate recovery to only 100% extension [Found: C, 85·3, 85·2, 85·4; H, 11·8, 11·8, 11·7; *M* (Rast), 1085, 1116, 1192; mean, 1131. $C_{80}H_{130}(OH)_2$ requires C, 85·3; H, 11·8%; *M*, 1125]. It has not a definite m. p., but softens progressively up to 100°, at which temperature it is a highly viscous, deep yellow fluid. In this condition it slowly oxidises in air (Found: Increase in weight after 24 and 48 hours at 100°, 0·29 and 2·07% respectively). It also slowly softens and oxidises in moist air at room temperature (28—32°). These reactions are being further investigated. Depressions of the freezing point of benzene solutions of caoutchol were measurable, but are probably of doubtful significance (cf. the discussion of a similar phenomenon by Pummerer, Andriessen, and Gündel, *Ber.*, 1929, **62**, 2628, in connection with raw rubber) (Found: *M*, 3200, 7000, 1608, 3216). The Menzies–Wright method was not applicable owing to the tendency of solutions to froth when boiling.

Caoutchol (1·6 g.) in benzene (20 c.c.) was heated under reflux for 30 minutes with acetic anhydride (4 c.c.). After removal of benzene, the product was treated with hot water and with hot alcohol to yield a brown tacky substance, *caoutchol diacetate* [Found: C, 83·6, 83·8; H, 11·6, 11·1; *M* (Rast), 1227 ± 70. $C_{80}H_{130}(O{\cdot}CO{\cdot}CH_3)_2$ requires C, 83·3; H, 11·3%; *M*, 1208].

(*b*) The filtrate. The faintly opalescent liquid resulting after removal of caoutchol was acidified with sulphuric acid. A strong mercaptan-like odour was detected and a flocculent buff-coloured solid separated. The latter, collected, dried, and weighed, constituted 2—3% of the crude caoutchol. It appears to be a complex mixture of carboxylic acids. The sulphur-containing substance is retained in the aqueous filtrate, which has been shown to contain a small amount of a highly reactive substance. Further investigation is proceeding.

Viscosity measurements were made in the Höppler research instrument at 26—29°.

The author is indebted to the Board of this Institute for permission to publish this and the preceding paper.

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## 43. *Derivatives of* cis-*3-Hydroxy-$\Delta^5$-cholenic Acid.*

By G. A. D. Haslewood.

*cis*-3-Hydroxy-$\Delta^{5:7}$-choladienic acid, the "cholanic acid analogue of ergosterol," has been obtained by the action of dimethylaniline on methyl 3 : 7-dibenzoyloxy-$\Delta^5$-cholenate. The last substance was prepared from methyl *cis*-7-keto-3-acetoxy-$\Delta^5$-cholenate, obtained (together with methyl 6-keto-3 : 5-diacetoxycholanate) by chromic acid oxidation of methyl *cis*-3-acetoxy-$\Delta^5$-cholenate. The dimethylaniline method of introducing a $C_{7-8}$ double bond into the sterol nucleus is here definitely superior to

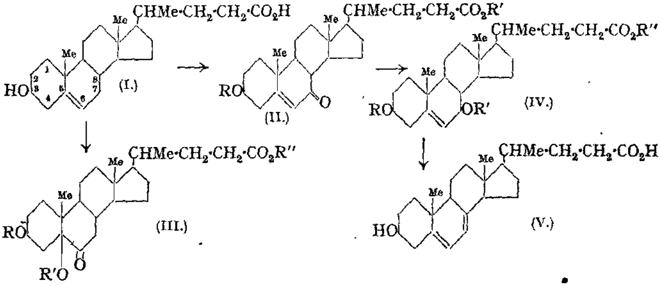
pyrolysis, which chiefly yielded crystalline substances of unknown constitution. Acids corresponding to the above esters have been prepared and characterised. *cis*-3-Hydroxy-Δ$^{5:7}$-choladienic acid and its water-soluble salts will be tested for antirachitic provitamin activity.

THE acetate of the methyl ester of *cis*-3-hydroxy-Δ$^5$-cholenic acid (I), obtained from cholesteryl acetate dibromide (Wallis and Fernholz, *J. Amer. Chem. Soc.*, 1935, **57**, 1504; Ruzicka and Wettstein, *Helv. Chim. Acta*, 1935, **18**, 986; Butenandt, Dannenbaum, and Hanisch, *Z. physiol. Chem.*, 1935, **237**, 57), has been oxidised by the chromic acid method employed by German workers for the acetates of cholesterol (Windaus, Lettré, and Schenck, *Annalen*, 1935, **520**, 98), stigmasterol (Linsert, *Z. physiol. Chem.*, 1936, **241**, 125), and sitosterol (Wunderlich, *ibid.*, p. 116).

In addition to the expected *methyl* cis-*7-keto-3-acetoxy-Δ*$^5$*-cholenate* * (II; R = $CO{\cdot}CH_3$, R′ = $CH_3$), there was obtained a saturated ketodiacetoxy-ester, which is probably a *methyl 6-keto-3 : 5-diacetoxycholanate* (III; R = R′ = $CO{\cdot}CH_3$, R″ = $CH_3$). This substance on hydrolysis gave (probably) a *6-keto-3 : 5-dihydroxycholanic acid* (III; R = R′ = R″ = H), characterised by a *monoacetyl methyl* ester and a *monosemicarbazone*. The corresponding cholestane ketodiacetoxy-compound, hydrolysable to a dihydroxyketone, was obtained in an analogous manner by Schenck (*Z. physiol. Chem.*, 1936, **243**, 119) from cholesteryl acetate, and was shown by him to be 6-keto-3 : 5-diacetoxycholestane.

Methyl *cis*-7-keto-3-acetoxy-Δ$^5$-cholenate [which on hydrolysis gave cis-*3-hydroxy-7-keto-Δ*$^5$*-cholenic acid* (II; R = R′ = H), characterised by a *semicarbazone*] was converted by aluminium *iso*propoxide into a *methyl 3 : 7-dihydroxy-Δ*$^5$*-cholenate* (IV; R = R′ = H, R″ = $CH_3$), hydrolysable to a 3 : 7-*dihydroxy-Δ*$^5$*-cholenic acid* (IV; R = R′ = R″ = H). Benzoylation of the crude, partly hydrolysed reduction product gave the *dibenzoate* (IV; R = R′ = $CO{\cdot}C_6H_5$, R″ = $CH_3$) of methyl 3 : 7-dihydroxy-Δ$^5$-cholenate.

Pyrolysis of this dibenzoate, by the method used by the German workers for the corresponding derivatives of cholesterol, stigmasterol, and sitosterol (Windaus *et al.*, Linsert, Wunderlich, *locc. cit.*), gave chiefly a crystalline *substance*, hydrolysed to an *acid*, $C_{24}H_{38\ (or\ 40)}O_4$, which was precipitable by digitonin. This acid and the parent substance showed no sterol colour reactions. The products of the pyrolysis, after saponification, yielded, further, a dihydroxy-acid, apparently impure 3 : 7-dihydroxy-Δ$^5$-cholenic acid, and also a very small amount of *cis*-3-hydroxy-Δ$^{5:7}$-choladienic acid (V).



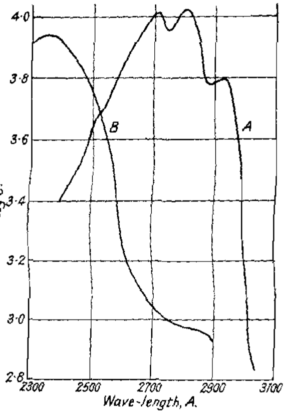

When, however, the dibenzoate of methyl 3 : 7-dihydroxy-Δ$^5$-cholenate was refluxed with dimethylaniline, the crystalline product obtained, which was readily isolated,

* At about the time that this substance and the corresponding acid were obtained, the author learned privately that they had been independently prepared by F. S. Spring and E. R. H. Jones, in collaboration with Professor I. M. Heilbron. The author wishes to express his appreciation of the open discussion which then took place with these workers on the problems connected with this research.

yielded on hydrolysis only cis-3-*hydroxy*-$\Delta^{5:7}$-*choladienic acid* (V), which was characterised by its *acetyl methyl* ester. The dimethylaniline method was found to be applicable also to the preparation of 7-dehydrocholesterol from the dibenzoate of 7-hydroxycholesterol.

The acid (V), which was the substance chiefly sought in this research, showed the colour reactions characteristic of ergosterol. Its absorption spectrum (curve *A*, for which, as also for curve *B*, the author is indebted to Professor C. W. Small) is very similar to that of ergosterol and shows maxima at 2710, 2810, and 2935 A.

Curve *B* shows the absorption spectrum of *cis*-3-hydroxy-7-keto-$\Delta^5$-cholenic acid.




A. cis-3-*Hydroxy*-$\Delta^{5:7}$-*choladienic acid.*
B. cis-3-*Hydroxy*-7-*keto*-$\Delta^5$-*cholenic acid.*
*Ethyl alcohol solutions.*

## Experimental.

All melting points are uncorrected. * denotes micro-analysis by Dr. I. A. Schoeller. Optical rotations were carried out in a 0·5 dm. Fischer micro-tube. Ethereal solutions were dried with anhydrous sodium sulphate. Compounds marked † were precipitable by digitonin.

*Purification of* cis-3-*Hydroxy*-$\Delta^5$-*cholenic Acid* (I).—Insoluble sodium salts from the debrominated acid fraction of the oxidation of cholesteryl acetate dibromide were hydrolysed with boiling alcoholic sodium hydroxide. The washed and dried ethereal extract of the diluted acidified product was evaporated, and the residue dissolved in a little fresh ether. The crystals separating were washed with ether and recrystallised from dilute alcohol containing benzene. This product (20 g.) in alcohol (1 l.) was treated with an excess of diazomethane, and the solvent evaporated. The residue, in pyridine (50 ml.), was heated at 100° for 30 minutes with acetic anhydride (50 ml.), and the product precipitated with water. Methyl *cis*-3-acetoxy-$\Delta^5$-cholenate formed white needles (21 g.), m. p. 154—157°, from dilute alcohol.

cis-3-*Hydroxy*-7-*keto*-$\Delta^5$-*cholenic Acid and Derivatives* (II).—The above acetoxy methyl ester (20 g.) in acetic acid (500 ml.) was stirred at 60° and treated with a solution of chromic oxide (16 g.) in acetic acid (180 ml.) and water (20 ml.), added during 1 hour. The temperature was kept at 55—60° for a further 3 hours, and the mixture then poured into much water and kept overnight. A solution of the precipitate in ether was washed with water, dilute sodium carbonate solution, and water, dried, and evaporated. From ethyl alcohol (200 ml.) the residue deposited crystals (4·8 g.) of *methyl* cis-7-*keto*-3-*acetoxy*-$\Delta^5$-*cholenate* (II; R = CO·CH$_3$, R′ = CH$_3$), which on recrystallisation from ethyl alcohol formed long colourless needles, m. p. 177—178° (Found: C, 72·9; H, 9·1.* $C_{27}H_{40}O_5$ requires C, 72·9; H, 9·1%). This product (0·2 g.) in alcohol (15 ml.) and 2N-sodium hydroxide (5 ml.) was kept overnight. Dilution of the acidified solution then gave cis-3-*hydroxy*-7-*keto*-$\Delta^5$-*cholenic acid* † (II; R = R′ = H), which after crystallisation from benzene and dilute alcohol formed small colourless plates, m. p. 223—225° (Found: C, 74·0; H, 9·2.* $C_{24}H_{36}O_4$ requires C, 74·2; H, 9·35%). $[\alpha]_D^{19°}$ − 115° ($c$ = 0·812, in ethyl alcohol). The acid gave a yellow colour in the Liebermann–Burchard reaction. The *semicarbazone* formed white crystals, decomp. 267—269°, from dilute alcohol (Found: N, 9·3. $C_{25}H_{39}O_4N_3$ requires N, 9·4%).

3 : 5-*Dihydroxy*-6-*ketocholanic Acid and Derivatives* (III).—The alcoholic liquors from the first crystallisation of methyl *cis*-7-keto-3-acetoxy-$\Delta^5$-cholenate were diluted with water and filtered from the first gummy precipitate. The filtrate, on further dilution, gave crystals (1·2 g.), m. p. 161—168°, of *methyl* 6-*keto*-3 : 5-*diacetoxycholanate* (III; R = R′ = CO·CH$_3$, R″ = CH$_3$), which, recrystallised from methyl alcohol, benzene–light petroleum, and ethyl alcohol, gave colourless needles of constant m. p. 172—173° (Found: C, 69·2; H, 8·8.* $C_{29}H_{44}O_7$ requires C, 69·0; H, 8·9%). When the crude product (0·2 g.) was kept in solution

in alcohol (6 ml.) and 2N-sodium hydroxide (5 ml.), crystals of sodium salt appeared. After 5 hours, these were collected, washed with alcoholic sodium hydroxide, and dissolved in water. Acidification gave 3 : *5-dihydroxy-6-ketocholanic acid* † (III; R = R′ = R″ = H), which formed long colourless needles, m. p. 278—279°, from dilute alcohol (Found: C, 71·1, 70·9; H, 9·3, 9·4.* $C_{24}H_{38}O_5$ requires C, 70·9; H, 9·4%). $[\alpha]_D^{19°}$ − 38° (*c* = 0·648, in ethyl alcohol). The acid gave a deep red colour in the Liebermann–Burchard reaction, and did not decolourise bromine in chloroform. The acid (0·3 g.) in alcohol was treated with an excess of diazomethane, and the solvent evaporated. The residue was heated at 100° in acetic anhydride (1 ml.) for 20 minutes. Dilution with water precipitated *methyl 5-hydroxy-6-keto-3-acetoxycholanate*, which crystallised from alcohol in colourless needles, m. p. 203—204° (Found: C, 69·9; H, 9·1.* $C_{27}H_{42}O_6$ requires C, 70·1; H, 9·2%). 3 : *5-Dihydroxy-6-ketocholanic acid monosemicarbazone* crystallised from alcohol in glistening needles, decomp. 267—269° (Found: N, 8·8.* $C_{25}H_{41}O_5N_3$ requires N, 9·1%).

3 : *7-Dihydroxy-$\Delta^5$-cholenic Acid and Derivatives* (IV).—A mixture of methyl *cis*-7-keto-3-acetoxy-$\Delta^5$-cholenate (1·8 g.), *iso*propyl alcohol (12 ml.), and freshly distilled aluminium *iso*propoxide (0·8 g.) was partly distilled during 8 hours. The yellow solution was cooled and treated with a solution of potassium hydroxide (1 g.) in methyl alcohol (15 ml.). After 30 minutes, the mixture was poured into water (200 ml.), and the precipitate collected and washed. (The filtrate on acidification gave a small quantity of crude acid, which was methylated with diazomethane, dissolved in ether, and precipitated with light petroleum as for the main fraction.) An ethereal solution of the precipitate was washed with water, dried, filtered, and evaporated to small volume. On addition of light petroleum, there was formed a precipitate (1 g.) of *methyl 3 : 7-dihydroxy-$\Delta^5$-cholenate* † (IV; R = R′ = H; R″ = $CH_3$), which crystallised from dilute alcohol in long white needles, m. p. 142—144° (Found: C, 74·6; H, 9·7.* $C_{25}H_{40}O_4$ requires C, 74·2; H, 10·0%). The crude light petroleum precipitate (1 g.), in pyridine (6 ml.), was treated gradually with benzoyl chloride (3 ml.) and kept at 0° for 24 hours. The mixture was diluted with water, and a washed and dried ethereal extract evaporated. With methyl alcohol, the oily residue gave crystals (0·8 g.) of the *dibenzoate* of methyl 3 : 7-dihydroxy-$\Delta^5$-cholenate. Recrystallisation from benzene–light petroleum and methyl alcohol–acetone gave long white needles, m. p. 165—166° (Found: C, 76·4; H, 7·9.* $C_{39}H_{48}O_6$ requires C, 76·4; H, 7·9%). Hydrolysis of this compound yielded 3 : *7-dihydroxy-$\Delta^5$-cholenic acid* † (IV; R = R′ = R″ = H), which crystallised from dilute alcohol in small white needles, m. p. 188—190° (decomp.) (Found: C, 73·55; H, 9·7.* $C_{24}H_{38}O_4$ requires C, 73·8; H, 9·8%). $[\alpha]_D^{19°}$ − 54° (*c* = 0·768, in ethyl alcohol). This acid and its derivatives gave a blue colour, changing to purple, in the Liebermann–Burchard reaction, and an intense blue colour with antimony trichloride in chloroform. Treatment of the above methyl ester with acetic anhydride in pyridine gave white needles, m. p. 161—164°, which showed no colour reactions.

*Pyrolysis of the Dibenzoate.*—The dibenzoate was heated at 195—200°/0·1 mm. for 1 hour. The following were representative experiments:—

(a) The pure dibenzoate (80 mg., m. p. 164—166°) gave a crystalline *product* (70 mg.), which was recrystallised from benzene–light petroleum and ethyl alcohol, forming white needles, m. p. 165—166° (Found: C, 75·7, 75·8; H, 8·4, 8·1%*). Treatment of this substance for 24 hours at room temperature with ethyl alcohol (10 ml.) and N-sodium hydroxide (1 ml.) gave on acidification colourless needles,† m. p. 214—216°, which, like the parent compound, showed no colour reactions (Found: C, 73·6; H, 9·3.* $C_{24}H_{38}O_4$ requires C, 73·8; H, 9·8%).

(b) From the crude dibenzoate (0·3 g.) was obtained, after purification from light petroleum, a product (0·15 g.), m. p. 136—145°, which was dissolved in alcohol (10 ml.) and left for 16 hours with 2N-sodium hydroxide (1 ml.). The mixture was diluted, acidified (acetic acid), and ether-extracted. The insoluble salts obtained on washing the ether with 2N-sodium hydroxide were collected and dissolved in water, and the acidified solution re-extracted with ether. The residue from the evaporation of the washed and dried extract gave, with a little benzene, long needles (80 mg.), m. p. 141—143° after recrystallisation from dilute alcohol. The substance † gave blue ⟶ purple Liebermann–Burchard, and blue antimony trichloride reactions (Found: C, 73·4; H, 8·6%*).

(c) In another experiment, the final product from the above treatment of the crude dibenzoate (0·4 g.) was a few mg. of (V), m. p. 205—210°.

cis-*3-Hydroxy-$\Delta^{5:7}$-choladienic Acid* (V).—The dibenzoate (0·2 g.) was refluxed for 8 hours with freshly distilled dimethylaniline (5 ml.). The cooled solution was poured into dilute hydrochloric acid and extracted with ether, and the washed and dried extract evaporated.

The residue separated from methyl alcohol in white crystals (80 mg.), which were refluxed for 15 minutes with alcohol (10 ml.) and 2N-sodium hydroxide (1 ml.). The cooled diluted acidified mixture was ether-extracted, and the extract washed with sodium hydroxide solution and with water. Evaporation of the washed and dried ethereal extract of the acidified washings gave white crystals, which were recrystallised from alcohol–benzene and from dilute alcohol, from which cis-3-*hydroxy*-$\Delta^{5:7}$-*choladienic acid* † (V) formed long white needles, m. p. 214—216° (decomp.) (Found: C, 77·1; H, 9·6.* $C_{24}H_{36}O_3$ requires C, 77·4; H, 9·75%). $[\alpha]_D^{19°}$ − 69° (*c* = 0·679, in ethyl alcohol). This substance (30 mg.), in alcohol, was treated with an excess of diazomethane, and the solvent removed. The residue, in pyridine (0·5 ml.), was heated with acetic anhydride (0·5 ml.) for 20 minutes at 100°. Precipitation of the cooled mixture with water gave *methyl* cis-3-*acetoxy*-$\Delta^{5:7}$-*choladienate*, which crystallised from methyl alcohol in white needles, m. p. 125—127° (Found: C, 75·2; H, 9·35.* $C_{27}H_{40}O_4$ requires C, 75·65; H, 9·4%). The choladienic acid and its acetyl methyl ester gave a deep blue ⟶ purple colour in the Liebermann–Burchard reaction, a bluish-green colour with antimony trichloride in chloroform, and an intense Tortelli–Jaffé reaction.

The author is extremely grateful to Dr. Karl Miescher, of Ciba, Basle, for the gift of a considerable quantity of the crude acids obtained by oxidation of cholesteryl acetate dibromide, which provided most of the starting material for this work.

British Postgraduate Medical School, London. [*Received, December* 22*nd*, 1937.]

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## 44. *Aluminium Chloride, a New Reagent for the Condensation of β-Ketonic Esters with Phenols. Part I. The Condensations of Methyl β-Resorcylate, β-Resorcylic Acid, and Resacetophenone with Ethyl Acetoacetate.*

By S. M. Sethna, N. M. Shah, and R. C. Shah.

Ethyl acetoacetate condenses with methyl β-resorcylate in presence of aluminium chloride with the formation of *methyl* 5-*hydroxy*-4-*methylcoumarin*-6-*carboxylate*, and with β-resorcylic acid to give the corresponding coumarin-6-carboxylic acid. The constitution of the coumarin ester has been determined by its degradation to 5-hydroxy-4-methylcoumarin, the coumarin structure of which is established by the formation of the methoxycinnamic acid derivative by Robertson and Canter's method. Resacetophenone, condensed similarly, affords 5-*hydroxy*-6-*acetyl*-4-*methylcoumarin*, the constitution of which is established by its identity with the product of the Fries transformation of 5-acetoxy-4-methylcoumarin and by the formation of a chromone. The smooth formation, in the above condensations, of 5-hydroxycoumarin derivatives, which are otherwise difficultly accessible, is of interest, as other condensing agents give 7-hydroxycoumarin derivatives.

The condensation of β-ketonic esters with phenols has been extensively studied in recent years, the principal condensing agents being concentrated sulphuric acid (Pechmann reaction) (*Ber.*, 1883, **16**, 2119) and phosphoric oxide (Simonis reaction) (*Ber.*, 1913, **46**, 2015). Zinc chloride, hydrogen chloride, phosphoryl chloride, phosphoric acid, and sodium ethoxide also have been used (Naik, Desai, and Desai, *J. Indian Chem. Soc.*, 1929, **6**, 801; Chakravarti, *ibid.*, 1935, **12**, 536; Appel, J., 1935, 1031), with results of no particular interest; phosphoryl chloride, however, acts in some cases like phosphoric oxide (Goodall and Robertson, J., 1936, 426).

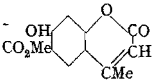
Clayton (J., 1908, **93**, 2016) stated that negative substituents, such as carboxyl and carbethoxyl, in a phenol inhibit Pechmann's coumarin condensation. Two of us (S.M.S. and R.C.S.), however, have condensed methyl β-resorcylate with ethyl acetoacetate in presence of sulphuric acid and obtained methyl 7-hydroxy-4-methylcoumarin-6-carboxylate (I) (under publication), the constitution of which was established by hydrolysis and subsequent decarboxylation to the 7-hydroxy-4-methylcoumarin, m. p. 185°, of Pechmann and Duisberg (*Ber.*, 1883, **16**, 2119). In an examination of other

possible condensing agents, the authors found that anhydrous aluminium chloride acted efficiently, the main product being *methyl 5-hydroxy-4-methylcoumarin-6-carboxylate* (II, R = Me), m. p. 185—186°, accompanied by a small quantity of methyl 7-hydroxy-4-methylcoumarin-6-carboxylate (I), m. p. 212—214°, whose identity with the product obtained by the sulphuric acid method was established by direct comparison. The new ester, m. p. 185—186°, on hydrolysis gave an acid, $C_{11}H_8O_5$, m. p. 244°, which on decarboxylation gave a compound, $C_{10}H_8O_3$, m. p. 263°. The decarboxylated product, which may be a hydroxymethyl-coumarin or -chromone, was definitely shown to be a coumarin derivative by the formation of a methylated cinnamic acid, $C_{12}H_{14}O_4$, by Robertson and Canter's method (J., 1931, 1875). The possibility of the substance being 7-hydroxy-2-methylchromone (m. p. 249—250°; Bloch and Kostanecki, *Ber.*, **1900, 33,** 471) or 5-hydroxy-2-methylchromone (m. p. 92°; Limaye and Kelkar, *Rasāyanam*, **1936, 1,** 28; *Abstr.*, 1937, *A*, ii, 257) is thus excluded. Of the two alternative constitutions, 7-hydroxy-4-methylcoumarin and 5-hydroxy-4-methylcoumarin, the latter (IV) undoubtedly represents the decarboxylated product, as the former compound is known and has m. p. 185° and also because the ester (II), m. p. 185—186°, is different from methyl 7-hydroxy-4-methylcoumarin-6-carboxylate (I), m. p. 212—214°, as previously mentioned. Limaye and Kelkar have recently reported the formation of 5-hydroxy-4-methylcoumarin, m. p. 263°, as a by-product in minute yield in the Kostanecki acetylation of 2-acetylresorcinol (which can only give a 5-hydroxy-compound), the main product being 5-hydroxy-3-acetyl-2-methylchromone, m. p. 122°, from which 5-hydroxy-2-methylchromone, m. p. 92°, was obtained by the action of alkali (*Rasāyanam*, **1936, 1,** 27, 47; *Abstr.*, 1937, *A*, ii, 254, 257). Our melting points for 5-hydroxy-4-methylcoumarin, its acetyl derivative, and its methyl ether agree with those recorded by these authors. The melting point of our 5-hydroxy-4-methylcoumarin was not depressed by a specimen kindly supplied by Prof. Limaye. Our m. p. 148—150° for the methylated *cinnamic acid* (V), however, differs from the m. p. 185° given by Limaye, the difference being probably due to *cis-trans* isomerism.

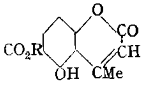
The constitution 5-hydroxy-4-methylcoumarin (IV) for the decarboxylated product leads to the alternative structures, *5-hydroxy-4-methylcoumarin-6-carboxylic acid* (II, R = H) and 5-hydroxy-4-methylcoumarin-8-carboxylic acid (III), for the carboxylic acid, m. p. 244°. The structure (II, R = H) is assigned, as the acid and the ester both give an intense violet coloration with alcoholic ferric chloride. 5-Hydroxy-4-methylcoumarin gives no ferric chloride reaction; only the 6-carboxylic acid, as an *o*-hydroxybenzoic acid, would give it, and not the 8-carboxylic acid, which would correspond to a *p*-hydroxybenzoic acid. This is supported by analogy, as the similar condensation with resacetophenone, described later, yields *5-hydroxy-6-acetyl-4-methylcoumarin* (VI), the structure of which as a 6-acetyl compound has been definitely establised by chromone formation.

β-Resorcylic acid was similarly condensed with ethyl acetoacetate, the product being 5-hydroxy-4-methylcoumarin-6-carboxylic acid (II, R = H), identical with the acid obtained by the hydrolysis of (II, R = Me).

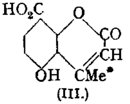
The condensation of methyl β-resorcylate with ethyl acetoacetate in presence of freshly fused zinc chloride gave a mixture consisting mainly of the 7-hydroxy-compound (I) together with a minute quantity of (II, R = Me).




(I.)

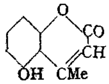


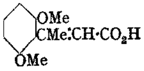

(II.)




(III.)

(IV.)



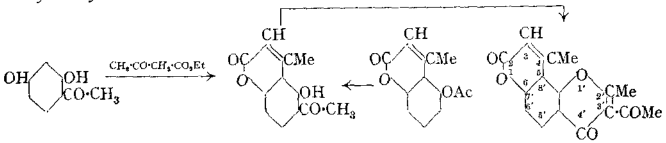




(V.)

With anhydrous aluminium chloride as condensing agent, resacetophenone condensed with ethyl acetoacetate, similarly to methyl β-resorcylate, the product, obtained in high yield, being exclusively 5-hydroxy-6-acetyl-4-methylcoumarin (VI), m. p. 165°.

The observation of Agarwal and Dutt (*J. Indian Chem. Soc.*, 1937, **14**, 109) that resacetophenone condenses with ethyl acetoacetate in the presence of sulphuric acid or sodium ethoxide, giving 7-hydroxy-6-acetyl-4-methylcoumarin, m. p. 147°, could not be confirmed, only unchanged resacetophenone being obtained in both cases. Desai and Hamid have recently carried out the same condensation in the presence of phosphoryl chloride and obtained 7-hydroxy-6-acetyl-4-methylcoumarin, m. p. 210° (*Proc. Indian Acad. Sci.*, 1937, **6**, 185).

The constitution (VI) for our condensation product, m. p. 165°, which dissolves in alkali with a deep yellow colour without fluorescence indicative of a 5-hydroxycoumarin, rests on the following grounds: (i) the Fries transformation of 5-acetoxy-4-methylcoumarin (VII) gave a compound, m. p. 164—165°, identical in all respects with the condensation product; (ii) it gives a strong ferric chloride reaction; (iii) acetylation with sodium acetate and acetic anhydride gives an acetylchromone, 3'-*acetyl*-4 : 2'-*dimethylchromono*-7' : 8' : 6 : 5-α-*pyrone* (VIII); benzoylation gave the flavone, 3'-*benzoyl*-2'-*phenyl*-4-*methylchromono*-7' : 8' : 6 : 5-α-*pyrone*. Clemmensen reduction of (VI) gave 5-*hydroxy*-4-*methyl*-6-*ethylcoumarin*.




(VI.) (VII.) (VIII.)

## Experimental.

*Condensation of Methyl β-Resorcylate with Ethyl Acetoacetate in Presence of Anhydrous Aluminium Chloride: Formation of Methyl 5-Hydroxy-4-methylcoumarin-6-carboxylate* (II, R = Me).—Anhydrous methyl β-resorcylate (Robinson and Shah, J., 1934, 1496) (20 g.; 1 mol.) and ethyl acetoacetate (17 g.; 1·1 mols.) were dissolved in hot dry nitrobenzene (20 c.c.) and a solution of anhydrous aluminium chloride [32 g.; 2 mols. (less or more than 2 mols diminished the yield)] in 120 c.c. of hot dry nitrobenzene added. The mixture, protected from moisture, was heated at 125—130° for about an hour until the evolution of hydrogen chloride was negligible; it was then cooled, ice and concentrated hydrochloric acid (10 c.c. added, and the nitrobenzene distilled in steam. The brown solid left was collected and refluxed with sufficient rectified spirit to dissolve about half of it.

The insoluble portion crystallised from rectified spirit in needles (5 g.), m. p. 185—186° of *methyl* 5-*hydroxy*-4-*methylcoumarin*-6-*carboxylate* (Found: C, 61·4; H, 4·4. $C_{12}H_{10}O$ requires C, 61·5; H, 4·3%). The m. p. was depressed 20° by the 7-hydroxy-isomer (I) The substance was sparingly soluble in alcohols, benzene, light petroleum, and 10% sodium hydroxide solution, more soluble in acetone, chloroform, and glacial acetic acid. It gave with alkali a deep yellow colour without fluorescence, characteristic of 5-hydroxycoumarins (Colli and Chrystall, J., 1907, **91**, 1804; Dey, J., 1915, **107**, 1614, 1621).

The substance obtained from the initial solution in rectified spirit was a mixture (about 5 g.). It was ground with 10% sodium hydroxide solution (35 c.c.). The insoluble portion crystallised from rectified spirit in needles (about 3 g.), m. p. and mixed m. p. with methyl 5-hydroxy-4-methylcoumarin-6-carboxylate 175—186°. Total yield of (II, R = Me), 8 g. The alkaline filtrate on acidification gave a product which crystallised from rectified spirit in needles (0·5 g.), m. p. and mixed m. p. with (I) 212—214°. It gave with alkali the blue fluorescence characteristic of 7-hydroxycoumarin derivatives, and a violet coloration with ferric chloride.

The *acetyl* derivative of (II, R = Me), prepared by refluxing the substance (0·5 g.) with acetic anhydride (4 c.c.) and pyridine (1 c.c.) for 2 hours, crystallised from dilute alcohol i

needles, m. p. 153—155° (Found: C, 60·7; H, 4·3. $C_{14}H_{12}O_6$ requires C, 60·9; H, 4·3%). The *benzoyl* derivative crystallised from alcohol in needles, m. p. 164—166° (Found: C, 67·4; H, 4·2. $C_{19}H_{14}O_6$ requires C, 67·45; H, 4·1%). The *methyl* ether, prepared by refluxing a solution of the ester (0·5 g.) in acetone (50 c.c.) for 20 hours with potassium carbonate (1 g.) and methyl iodide (3 c.c.), crystallised from rectified spirit in long needles (0·4 g.), m. p. 106—107° (Found: C, 62·8; H, 5·0. $C_{13}H_{12}O_5$ requires C, 62·9; H, 4·8%); it was insoluble in alkali and did not give a ferric chloride reaction.

*5-Hydroxy-4-methylcoumarin-6-carboxylic Acid* (II, R = H).—(A) The ester (II, R = Me) (2 g.) was heated in a sealed tube with glacial acetic acid (20 c.c.) and concentrated hydrochloric acid (15 c.c.) for 3 hours at 130—140°. The separated product crystallised from rectified spirit in needles (1·5 g.), m. p. 244° (efferv.) (Found: C, 58·5; H, 3·8. $C_{11}H_8O_5,0·25H_2O$ requires C, 58·7; H, 3·8%). (B) The above ester (0·5 g.) was shaken with 10% sodium hydroxide solution (20 c.c.) and kept for 60 hours; the substance obtained on acidification crystallised from alcohol in needles (0·25 g.), m. p. and mixed m. p. with the product from (A) 244° (efferv.).

The *acid* formed sparingly soluble sodium and potassium salts. It readily dissolved in caustic alkali with a yellow colour without fluorescence and, like its methyl ester, gave an intense violet coloration with alcoholic ferric chloride. Acetyl and benzoyl derivatives could not be prepared by the usual methods.

*5-Hydroxy-4-methylcoumarin* (IV).—The ester (II, R = Me) (2 g.) was heated with water (15 c.c.), glacial acetic acid (15 c.c.), and concentrated hydrochloric acid (10 c.c.) in a sealed tube for 6—7 hours at 180—185°. The product crystallised from dilute alcohol in needles (1 g.), m. p. 263° (Found: C, 67·9; H, 4·5. Calc. for $C_{10}H_8O_3$: C, 68·2; H, 4·55%).

The acid (II, R = H) can be decarboxylated quantitatively by heating it until it melts. 5-Hydroxy-4-methylcoumarin is soluble in alcohols, acetic acid, and acetone and sparingly soluble in chloroform, benzene, and light petroleum. It gives an intense yellow colour with alkali.

The acetyl derivative crystallised from benzene in needles, m. p. 112—114° (Found: C, 66·0; H, 4·75. Calc. for $C_{12}H_{10}O_4$: C, 66·1; H, 4·6%). The *benzoyl* derivative crystallised from alcohol in needles, m. p. 175—177° (Found: C, 72·6; H, 4·4. $C_{17}H_{12}O_4$ requires C, 72·85; H, 4·3%). The methyl ether, prepared by means of methyl sulphate and cold sodium hydroxide solution and crystallised first from alcohol and then from benzene, had m. p. 140—142°. Limaye and Kelkar (*loc. cit.*) give m. p. 143° (Found: C, 69·4; H, 5·2. Calc. for $C_{11}H_{10}O_3$: C, 69·5; H, 5·3%).

*2 : 6-Dimethoxy-β-methylcinnamic Acid* (V).—The substance (IV) (0·7 g.) was refluxed for 15 minutes with 4% sodium hydroxide solution (15 c.c.), and methyl sulphate (2 c.c.) added. More of these two reagents were added and the mixture was heated on the water-bath for a few minutes and left overnight. The *product* obtained on acidification with hydrochloric acid was crystallised from 20% acetic acid and then from benzene–light petroleum; m. p. 148—150°. It decolourised bromine water and dilute permanganate solution and gave no coloration with ferric chloride (Found: C, 64·8; H, 6·2. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·3%).

*Condensation of β-Resorcylic Acid with Ethyl Acetoacetate in Presence of Aluminium Chloride.*—β-Resorcylic acid (10 g.), ethyl acetoacetate (10 g.), and aluminium chloride (17 g.) in dry nitrobenzene (70 c.c.) were heated at 115—120° for 1½ hours, and the mixture worked up as in the case of methyl β-resorcylate. The solid obtained, twice crystallised from rectified spirit, formed needles (2 g.), m. p. 244°, identical with the acid obtained by the hydrolysis of (II, R = Me). The mother-liquor gave a faint blue fluorescence with alkali, but no 7-hydroxycoumarin derivative could be isolated.

*Condensation of Methyl β-Resorcylate in Presence of Zinc Chloride.*—Methyl β-resorcylate (5 g.; 1 mol.), ethyl acetoacetate (5 g.; 1 mol.), and freshly fused zinc chloride (10 g.) were mixed, and heated for 1½ hours at 135—140°; after cooling, water and a few c.c. of hydrochloric acid were added. The product was collected and crystallised from rectified spirit; it was a mixture (m. p. 172—187°). On recrystallisation from benzene, crystals separated, m. p. and mixed m. p. with (I) 212—214°. The mother-liquor on evaporation gave a product which after two recrystallisations from benzene had m. p. and mixed m. p. with (II, R = Me) 184—185°.

*Condensation of Resacetophenone with Ethyl Acetoacetate in Presence of Anhydrous Aluminium Chloride: Formation of 5-Hydroxy-6-acetyl-4-methylcoumarin* (VI).—Resacetophenone (Robinson and Shah, J., 1934, 1494) (7·6 g.; 1 mol.) and ethyl acetoacetate (6·5 g.; 1 mol.) were added

to a solution of aluminium chloride (13·5 g.; 2 mols.) in dry nitrobenzene (80 c.c.) and the mixture treated as described on p. 230. The brown solid left after steam-distillation of the nitrobenzene crystallised from glacial acetic acid in needles; recrystallisation from boiling alcohol gave colourless needles (4—4·5 g.), m. p. 165° (Found: C, 65·7; H, 4·6. $C_{12}H_{10}O_4$ requires C, 66·0; H, 4·7%). *5-Hydroxy-6-acetyl-4-methylcoumarin* was easily soluble in chloroform and benzene, sparingly soluble in water and alcohol, and insoluble in light petroleum. It gave with alkali a deep yellow colour without fluorescence, and with alcoholic ferric chloride a deep cherry-red coloration.

The *acetyl* derivative, prepared by refluxing the substance (0·5 g.) with acetic anhydride (5 c.c.) and pyridine (1—2 c.c.) for 3 hours, crystallised from absolute alcohol in clusters of needles, m. p. 152° (Found: C, 64·0; H, 4·7. $C_{14}H_{12}O_5$ requires C, 64·6; H, 4·6%). The *phenylhydrazone*, crystallised from glacial acetic acid and then from alcohol, formed long, yellow, rectangular needles, m. p. 236—237° (Found: * N, 9·2. $C_{18}H_{16}O_3N_2$ requires N, 9·1%). The *oxime* crystallised from nitrobenzene in thin lustrous plates, m. p. 260° (decomp.) (Found: * N, 6·2. $C_{12}H_{11}O_4N$ requires N, 6·0%). The semicarbazone was sparingly soluble in the common organic solvents and separated from nitrobenzene in granular crystals, m. p. about 290° (decomp.).

*Fries Transformation of 5-Acetoxy-4-methylcoumarin*.—A mixture of the coumarin derivative (VII) (0·5 g.) and aluminium chloride (2·5 g.) was heated for 2 hours at 170—180° and cooled, and ice-water and a few drops of hydrochloric acid added. The solid that separated was crystallised from acetic acid and recrystallised from alcohol; it had m. p. 163—164°, alone or mixed with the condensation product (VI).

*3′-Acetyl-4 : 2′-dimethylchromono-7′ : 8′ : 6 : 5-α-pyrone* (VIII).—5-Hydroxy-6-acetyl-4-methylcoumarin (1 g.), acetic anhydride (20 c.c.), and anhydrous sodium acetate (3 g.) were heated together at 150—160° for 6—7 hours, the mixture cooled and poured into cold water, and the separated solid washed with water and with dilute sodium hydroxide solution. On crystallisation from alcohol it gave yellowish needles, m. p. 204°, of the *chromonopyrone* (VIII). It did not give a coloration with ferric chloride and was insoluble in cold aqueous sodium hydroxide, but formed a yellow solution on heating (Found: C, 67·6; H, 4·4. $C_{16}H_{12}O_5$ requires C, 67·6; H, 4·2%).

*3′-Benzoyl-2′-phenyl-4-methylchromono-7′ : 8′ : 6 : 5-α-pyrone*.—The coumarin (VI) (1 g.), benzoic anhydride (8 g.), and sodium benzoate (3 g.) were heated together at 180—190° for 9 hours. After the usual treatment with alcohol (25 c.c.) and potassium hydroxide (5 g.) and gentle heating, the solid *compound* obtained separated from pyridine or glacial acetic acid in tiny yellow crystals, m. p. 301° after shrinking (Found: C, 76·2; H, 4·0. $C_{26}H_{16}O_5$ requires C, 76·5; H, 3·9%).

*5-Hydroxy-4-methyl-6-ethylcoumarin*.—5-Hydroxy-6-acetyl-4-methylcoumarin (1 g.) was dissolved in alcohol, added to a mixture of zinc amalgam (prepared from 12 g. of zinc dust Robinson and Shah, J., 1934, 1497) and concentrated hydrochloric acid (30 c.c.), and heated on a boiling water-bath for about an hour; concentrated hydrochloric acid (5 c.c.) was then added, and heating continued for another hour. The filtrate from the unchanged amalgam on cooling, deposited needles, m. p. 172°, which were recrystallised from aqueous methyl alcohol; m. p. 174—175° (Found: C, 67·8; H, 6·1; loss at 100°, 4·0. $C_{12}H_{12}O_3,\frac{1}{2}H_2O$ requires C, 67·6; H, 6·1; $H_2O$, 4·2%). The *compound* did not give a ferric chloride reaction and dissolved in alkali with a deep yellow colour.

All the analyses recorded are microanalyses; those marked with an asterisk were done by Dr. J. N. Ray of Lahore, to whom our thanks are due, and the others by Dr. Schoeller.

A discussion of the mechanism of the formation of 5-hydroxycoumarin derivatives in these reactions is postponed pending further work on similar lines which is being carried out in view of the remarkable results described above.

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## 45. *The Constitution of the Nitrosopentammine Cobalt Salts.*

By (Mrs.) J. L. Milward, W. Wardlaw, and W. J. R. Way.

Some years ago an account was published of the preparation and properties of the so-called nitrosopentammine cobalt salts. Two series of salts were described, one being red and the other black. Both series were obtained by the action of nitric oxide on ammoniacal solutions of cobaltous salts and they have the same general formula [NO, Co, $5NH_3$]$X_2$. Various structures have been proposed to explain the striking differences in colour and chemical properties which these salts exhibit. The present authors bring forward chemical and physical evidence which they consider proves that the red compounds are true nitroso-derivatives [NO—Co,$5NH_3$]$X_2$ in which the 6-covalent cobalt is tervalent; the black compounds, on the other hand, although containing 6-covalent cobalt, have a structure in which the NO group resonates and leads to the formulæ [$5NH_3$,$\overset{=}{Co}$—$\overset{+}{N}$≡$\overset{+}{O}$]$X_2$ and [$5NH_3$,$\overset{-}{Co}$=$\overset{+}{N}$=O]$X_2$ whereby the principal valency of the cobalt changes from one to three.

The nature of the linkage formed between nitric oxide and a metallic atom has been much discussed. The obvious analogy between nitric oxide and carbon monoxide in the metallic nitrosyl and carbonyl compounds has led to the suggestion that they must be similarly constituted, but as nitric oxide has one more electron than carbon monoxide the assumption is generally made that this electron is contributed to the metal with which the NO is associated. Hieber and Anderson (*Z. anorg. Chem.*, 1932, **208**, 238; 1933, **211**, 132) consider that in the nitrosocarbonyls, such as $Co(CO)_3NO$, the NO group, having donated an electron to the metal, is then linked by a double electron-pair bond to the same metal, and that there is a double bond between the nitrogen and the oxygen atom, thus $\overset{-}{M}::\overset{+}{N}::\ddot{O}:$ or $\overset{-}{M}$=$\overset{+}{N}$=O. On the other hand, Sidgwick and Bailey (*Proc. Roy. Soc.*, 1934, *A*, **144**, 521) maintain that this idea leads to values for the principal valency and covalency of metal atoms which cannot be entertained. They suggest that the linking is $\overset{-}{M}:\overset{+}{N}:::O:$ or $\overset{=}{M}$—$\overset{+}{N}$≡$\overset{+}{O}$. In a recent investigation on the molecular structures of the nitrosocarbonyls of cobalt and iron by electron diffraction, Brockway and Anderson (*Trans. Faraday Soc.*, 1937, **33**, 1233) calculate that the metal–nitrogen distances are about 0·16 A. less than the corresponding single-bond distance, whilst the bond lengths in the nitroso- and carbonyl groups are intermediate between those of double and triple bonds. They conclude, therefore, that the structure of these compounds is in accordance with the resonating electronic structures (1) $\overset{=}{M}$—$\overset{+}{N}$≡$\overset{+}{O}$ and (2) $\overset{-}{M}$=$\overset{+}{N}$=O. This idea of a resonating electronic structure for the NO group appears to explain the constitution of that curious group of compounds, the black nitroso-pentammine cobalt salts. It has been known for many years (Sand and Geissler, *Ber.*, 1903, **36**, 2083; *Annalen*, 1903, **329**, 194) that by the action of nitric oxide on an ammoniacal solution of a cobaltous salt it is possible to isolate derivatives with the empirical formula [$5NH_3CoNO$]$X_2$ and that these derivatives may exist in black or red modifications. It has been found that when a cobaltous halide is used, the black series results, whereas if cobaltous nitrate is employed the red modification is generally obtained. The exact constitution of the black series had not been considered in detail until 1934 when Sidgwick and Bailey suggested (*loc. cit.*) that these salts were really true nitroso-derivatives [$5NH_3Co$—NO]$Cl_2$, where the cobalt atom is tervalent and 6-covalent as in [$5NH_3CoCl$]$Cl_2$. It is difficult, however, to reconcile this structure with the properties of the black salts. In the first place we have confirmed the fact (Werner and Karrer, *Helv. Chim. Acta*, 1918, **1**, 54) that the nitric oxide is very readily liberated as such when dilute hydrochloric acid or even water is added to the black chloride, and that, as a result of the decomposition with dilute acid, the cobalt is obtained in the form of cobaltous chloride. If the black chloride were actually the cobaltic salt [$5NH_3Co$—NO]$Cl_2$, decomposition with hydrochloric acid should yield the very stable purpureo-chloride [$5NH_3CoCl$]$Cl_2$, with liberation of $(NOH)_x$ possibly as hyponitrous acid or as water and nitrous oxide. Additional

evidence against the constitution suggested by Sidgwick and Bailey is the important fact that the black chloride is paramagnetic. Rây and Bhar (*J. Indian Chem. Soc.*, 1928, **5**, 497) carried out some preliminary magnetic measurements at 29° on this black chloride which indicated paramagnetism, and we have now shown that this is actually so by measurements over the temperature range − 195° to 85°. This seems to indicate quite clearly that the black chloride is not an ammine of tervalent cobalt, for all cobaltic complexes of the series $K_3[CoCl_6]$ to $[Co6NH_3]Cl_3$ are diamagnetic. A consideration of these experimental facts makes it most probable that in the black series of compounds the NO is attached to the metal atom by the same linkages as the NO group in the nitrosocarbonyls of the metals. This would mean that the structure contains a resonating NO group, which would lead to the formulæ $[5NH_3\overset{=}{Co}\overset{+}{N}\equiv\overset{+}{O}]Cl_2$ and $[5NH_3\overset{-}{Co}=\overset{+}{N}=O]Cl_2$. If the NO resonates between the structures proposed, then the principal valency of the cobalt would change from 1 to 3. The black colour of the chloride is quite in accordance with this idea, for it is generally accepted that substances showing an intermediate valency have a dark colour as in the familiar cases of the black thallo-thallic salts and the black cupro-cupric derivatives. The red salts, however, do appear to be true nitroso-compounds, as Sidgwick and Bailey suggest, but there seems no reason why they should be considered dimeric. Sand and Geissler (*loc. cit.*), who first prepared these compounds, formulated them as $(N_2O_2)[Co(NH_3)_5X_2]_2$ because the nitrate had half a molecule of water of crystallisation. It is now realised that this conclusion is unsound, for the water content will be determined by the crystal lattice. Moreover, Werner and Karrer (*loc. cit.*) could not isolate hyponitrous acid from these salts or detect it in solution. They also attempted to prepare the red salts by the action of silver hyponitrite on $[5NH_3CoCl]X_2$ but without success, and we now find, in accordance with their results, that the substance obtained from this reaction is an aquopentamminocobaltic salt. The idea that these red salts are true nitroso-derivatives agrees well with the experimental fact that by treatment with hydrochloric acid no nitric oxide is liberated, and that the purpureo-chloride $[5NH_3CoCl]Cl_2$ separates from the solution. Even more significant is the fact that the nitrate $[5NH_3CoNO](NO_3)_2$ is diamagnetic and in this respect takes its place as a typical member of the series of ammines of tervalent cobalt.

## EXPERIMENTAL.

*Black Nitrosopentamminocobalt Chloride.*—A hot solution of cobaltous chloride hexahydrate (25 g.; 50 c.c.) was added to ammonia (*d* 0·88; 125 c.c.) and then filtered into a nitrogen-filled flask. Nitric oxide was passed into this ammoniacal solution for about 3 hours, after which the reaction products were filtered off, and the black residue washed with ammonia (*d* 0·88), alcohol, and then ether, and dried over calcium chloride. This black crystalline powder could be kept for long periods, in the absence of moisture, without change in composition (Found: Co, 24·1; Cl, 28·8. Calc. for $[5NH_3CoNO]Cl_2$: Co, 24·0; Cl, 28·9%). The compound is insoluble in all organic solvents and is decomposed by water with liberation of nitric oxide. Addition of hydrochloric acid to the solid liberates nitric oxide and gives a blue solution characteristic of cobaltous salts.

*Red Nitrosopentamminocobalt Nitrate.*—A hot solution of hydrated cobalt nitrate (17 g.; 25 c.c.) was added to ammonia (*d* 0·88; 85 c.c.) and treated for several hours with nitric oxide as above. The solid product was filtered off and recrystallised from very dilute ammonia solution. After drying over calcium chloride the crystals still retained ½ $H_2O$ (Found: Co, 19·2; $NH_3$, 27·8. Calc. for $[5NH_3CoNO](NO_3)_2,0·5H_2O$: Co, 19·2; $NH_3$, 27·6%). This compound is insoluble in the ordinary organic solvents but soluble and stable in water. With cold concentrated hydrochloric acid it yields $[5NH_3CoCl]Cl_2$ (Found: Co, 23·6. Calc.: Co, 23·56%).

*Magnetic Susceptibility of Nitrosopentamminocobalt Chloride and Nitrate.*—*Chloride.* Measurements on the magnetic susceptibility of the two foregoing salts have been made for the temperature interval − 195° to 85° by means of the Gouy method, in which a glass tube containing the substance under investigation is suspended with its axis at right angles to a homogeneous magnetic field, one end of the tube being in the field and the other end in a region where the field is negligible. The force (in dynes) acting on the substance is $f = \frac{1}{2}(\kappa - \kappa_m)sH^2$, where $\kappa$ and $\kappa_m$ are the volume susceptibilities respectively of the substance and of the surrounding medium, $H$ is the value of the magnetic field, and $s$ the inside cross-section of the tube. The

force $f$ is determined by means of a balance sensitive to 0·02 mg. The tube is suspended in a slightly larger tube, which is itself surrounded by a Dewar flask where various baths maintain a constant temperature. Level with each end of the sample holder severally are two copper–constantan thermocouples. The glass tubes used for holding the substances were 10 cm. long; they were of special Jena glass with a precise inside diameter correct within 0·01 mm. They had an inside cross diameter of 3 or 4 mm. A correction is made for the magnetism of the tube itself.

The measurements were made at the temperature of liquid air and solid carbon dioxide and also for a range between 0° and 90°. The calibration of the apparatus was made with solid manganese sulphate, whose mass susceptibility is taken to be $\chi_s = +83·1 \times 10^{-6}$ at 16°, and also with cerous chloride hexahydrate, whose mass susceptibility is $6·06 \times 10^{-6}$ at 18°.

*Measurements at room temperature* (17°). In the following tables, $f$ is the force (in mg.) acting on the tube containing a column of length $l$ cm. of the substance under investigation, $f_s$, the force acting on the paramagnetic salt used as standard (manganese sulphate or cerous chloride) for the same length $l$, $f_t$ is the force exerted on the empty tube, $p$ and $p_s$ the weights (in g.) respectively of the ammine and of the standard substance, $\chi_1$ the gram susceptibility of nitrosopentamminocobalt chloride, and $\chi_s$ that of the standard. $\kappa_m$ being negligible compared with $\kappa$, $\chi_1$ is given by the formula $\chi_1 = fp_s\chi_s/f_sp$.

The data given below are believed to be accurate to 2—2·5%. The values obtained for $\chi_1$ are

| Diam. of tube, mm. | $l$. | $l_s$. | $f_t$. | $f$. | $p$. | $MnSO_4$. $f_s$. | $MnSO_4$. $p_s$. | $CeCl_3,6H_2O$. $f_s$. | $CeCl_3,6H_2O$. $p_s$. | $\chi_1 \times 10^6$. |
|---|---|---|---|---|---|---|---|---|---|---|
| 4 | 8·244 | 8·222 | −0·78 | 3·96 | 0·81562 | 124·30 | 1·1909 | — | — | 3·86 |
| 4 | 8·278 | 8·270 | −0·78 | 3·94 | 0·82126 | 120·41 | 1·1772 | — | — | 3·89 |
| 4 | — | 8·220 | −0·78 | 3·94 | 0·82126 | — | — | 12·94 | 1·73142 | 3·88 |

converted into molecular susceptibilities, $\chi_m$, by multiplying by the molecular weight 245. Correction must then be applied for the diamagnetism of the various atoms and radicals and for the underlying diamagnetism of the central cobalt ion itself. The value of this correction, $\alpha$, is computed from the following data by applying the Pascal formula: $\alpha = \Sigma\chi_A + \lambda$, where $\Sigma\chi_A$ represents the sum of the susceptibilities of all the atoms or radicals in the molecule and $\lambda$ is a constitutive correction constant depending on the nature of the chemical bond involved.

| | Cl. | $NO_3$. | $NO_2$. | $NH_3$. | $H_2O$. |
|---|---|---|---|---|---|
| $-\chi_A \times 10^6$ .............. | 21 | 19 | 13·6 | 15 | 13·5 |

It follows from investigations by Rosenbohm (*Z. physikal. Chem.*, 1919, **93**, 693) that the value of $\lambda$ is constant for each kind of ammine and is equal to $+60 \times 10^{-6}$ for all pentammines. The value of the total correction to be applied in the present case is $+72 \times 10^{-6}$, which is also that found experimentally by Rosenbohm for the diamagnetic susceptibility of the very similar compound $[Co(NH_3)_5NO_2]Cl_2$.

*Variation of magnetic susceptibility with temperature.* In the following table, $\chi_c$ is the susceptibility per gram-ion of cobalt corrected as explained before for the diamagnetism of the molecule.

| $T$ (K.). | $\chi_1 \times 10^6$. | $\chi_m \times 10^6$. | $\chi_c \times 10^6$. | $1/\chi_c$. | $T$ (K.). | $\chi_1 \times 10^6$. | $\chi_m \times 10^6$. | $\chi_c \times 10^6$. | $1/\chi_c$. |
|---|---|---|---|---|---|---|---|---|---|
| 70° | 12·04 | 2949 | 3021 | 331 | 289° | 4·10 | 1004 | 1076 | 929 |
| 89 | 10·44 | 2557 | 2629 | 380 | 290 | 3·90 | 955 | 1027 | 973 |
| 193 | 5·85 | 1433 | 1505 | 664 | 348·1 | 3·34 | 818 | 890 | 1123 |
| 284 | 4·21 | 1031 | 1103 | 907 | | | | | |

If the reciprocal, $1/\chi_c$ of the ionic susceptibility is plotted against the absolute temperature, a straight line is obtained. The variation of susceptibility follows a Curie–Weiss law $\chi_c(T + \Delta) = C$. We have for each experimental point the relation $1/\chi_c = T/C + \Delta/C$. The values of $C$ and $\Delta$ have been calculated by application of the principle of least squares to this set of relations, and found to be $C = 0·351$, $\Delta = 39·9$. If we calculate the Weiss magneton number as defined by the relation, $\mu_W = 14·07\sqrt{C}$, we find $\mu_W = 8·32$. For this substance at 29° Rây and Bhar (*loc. cit.*) record a value of 13·9 Weiss magnetons. They state, however, " that we did not take sufficient pains to obtain magnetically pure samples in all cases, especially in the case of certain unstable compounds." We have carried out determinations on a number of samples prepared at different times and they gave concordant results. As the Weiss magneton lacks theoretical significance, it is preferable to express the result in Bohr magnetons which, on the " spin only " rule, is given by the relationship 8·6 Weiss magnetons = 1·73 Bohr magnetons = the moment produced by one unpaired spin. The observed magnetism of this black compound is

difficult to interpret, for although cobaltic salts are diamagnetic, yet cobaltous compounds usually possess moments greater than that predicted for an electron spin of $\frac{3}{2}$, *viz.*, $\mu_{eff.}$ = 3·87 Bohr magnetons (Sugden and Barkworth, *Nature*, 1937, **139**, 375). The complicating feature in this instance is the nitric oxide molecule and it seems preferable to defer discussion of this interesting case till more data, relating to similar substances, are available.

*Nitrate.* Experiments at room temperature and with air as surrounding medium show that nitrosopentamminocobalt nitrate is diamagnetic. Two experiments were made which gave the values $\chi_1 = -0{\cdot}19 \times 10^{-6}$ and $-0{\cdot}11 \times 10^{-6}$ for the gram-susceptibility.

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# 46. *The Functional Relation between the Constants of the Arrhenius Equation. Solvent Effects in a Diels–Alder Addition.*

By R. A. Fairclough and C. N. Hinshelwood.

The dependence upon the polarity of the solvent of the term *PZ* in the reaction velocity equation $k = PZe^{-E/RT}$ in an example of the Diels–Alder addition is compared with that previously studied for quaternary ammonium salt formation. Since in highly polar solvents an increase in *PZ* at constant activation energy is still found, though of considerably diminished magnitude, the effect cannot be wholly explained as an increase in *P* due to the stabilisation of a polar product, but may be partly due to this and to an actual change in the collision frequency, *Z*.

In a previous communication (J., 1937, 1573) the rate of formation of methylpyridinium iodide in various solvents was studied, the results being analysed in terms of the equation $k = PZe^{-E/RT}$. The total variation of log *PZ* could be accounted for by assuming a general correlation between log *PZ* and *E*, together with a tendency for log *PZ* to increase in the more polar solvents. Two alternative kinds of explanation were indicated. On the one hand, individual molecules of the solvent might increase *P* by stabilising molecules of the polar product which would otherwise revert into their constituents (cf. Hinshelwood, *Trans. Faraday Soc.*, 1936, **32**, 970; 1938, **34**, 138). On the other hand, the conditions in a polar solvent might be such as to produce an actual increase in the frequency of the encounters between the reactant moelcules, *i.e.*, to increase *Z* itself.

The present experiments were designed in the hope of estimating the relative importance of these two factors. If the influence of the polar solvents is due to a stabilisation of a polar product then it should only be observed in reactions where such a product is formed, whereas if it depends upon changes in *Z* then it should be equally in evidence when the product is non-polar. The reaction chosen for investigation was the condensation of *cyclo*pentadiene with benzoquinone, which gives a product of very low polarity (Wassermann, J., 1935, 828). It was studied in carbon tetrachloride, benzene, nitrobenzene, and benzonitrile.

*cyclo*Pentadiene was prepared by the destructive distillation of di*cyclo*pentadiene in the presence of iron wire in an apparatus fitted with a Dufton column wound with nickel wire. The diene distilled over at 40°, and was collected in a small weighed tube of thin glass, which was sealed, weighed, and then broken under the surface of a known volume of solvent. Solutions were always used within a few hours, and usually within a few minutes, of preparation. In some experiments the diene was distilled in a current of dry oxygen-free nitrogen, and in others in air, but no difference in the reaction rate was observed.

Benzoquinone was recrystallised from hexane. Specially purified medicinal carbon tetrachloride was used: benzene, nitrobenzene, and benzonitrile were fractionated in an all-glass apparatus. The benzene had been dried over sodium, and the nitrobenzene over calcium chloride.

The rate of reaction was followed by the colorimetric method described by Wassermann. The decrease in colour as the quinone reacted was measured with a Zeiss Pulfrich Stufen photometer using filter S47. Equal volumes of solutions of the reactants, N/100 before mixing, were preheated, mixed, and placed in a 15-cm. all-glass polarimeter tube with a ground-glass

stopper. The tube was held in a small brass tank with glass windows, and water was circulated from an electrically controlled thermostat. A thermometer in the tank was found to vary by less than 0·1°. It was compared with an N.P.L. standard.

The logarithms of the readings on the scale of the photometer were found to be directly proportional to the concentration of the quinone. Readings were taken at frequent intervals during a run, and their logarithms plotted against time. From the best smooth curve drawn through these points, bimolecular constants were calculated. The reaction was found to follow the bimolecular law and the Arrhenius equation in each solvent. The rate was measured in benzene at five temperatures, and in other solvents at six, in the range 10—50°. All constants were corrected for solvent expansion. The following table shows typical experiments in benzene and in nitrobenzene.

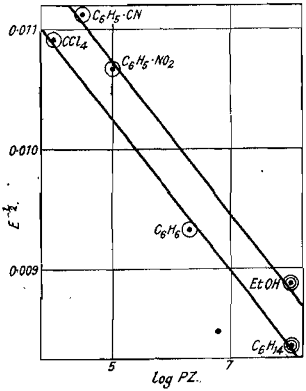
| Benzene; 27·2°. | | | Nitrobenzene; 40·8°. | | |
|---|---|---|---|---|---|
| Mins. | % changed. | *k*. | Mins. | % changed. | *k*. |
| 32 | 10 | 0·0118 | 7 | 10 | 0·0523 |
| 50 | 15 | 0·0120 | 10·5 | 15 | 0·0560 |
| 69 | 20 | 0·0121 | 14 | 20 | 0·0596 |
| 91 | 25 | 0·0122 | 19·2 | 25 | 0·0576 |
| 114 | 30 | 0·0125 | 24 | 30 | 0·0596 |
| 145 | 35 | 0·0123 | 29 | 35 | 0·0610 |
| 179 | 40 | 0·0124 | 35 | 40 | 0·0630 |
| 228 | 45 | 0·0119 | 135 | 70 | 0·0576 |
| 295 | 50 | 0·0113 | | | |
| Mean 0·0120 (l./g.-mol.)/sec., | | | Mean 0·0583 (l./g.-mol.)/sec., | | |

both uncorrected for solvent expansion.

Values of $E$ and log $PZ$ were calculated by the method of least squares. The "probable error" in $E$ was calculated and in each case was of the order 250 calories. The values obtained were as follows:

| Solvent. | *E*. | log *PZ*. | Solvent. | *E*. | log *PZ*. |
|---|---|---|---|---|---|
| Carbon tetrachloride ...... | 8,400 | 4·03 | Nitrobenzene .............. | 8,800 | 4·90 |
| Benzene ..................... | 11,500 | 6·31 | Benzonitrile .............. | 8,000 | 4·50 |

The values for carbon tetrachloride and benzene agree with those obtained by Wassermann (*J.*, *1936*, *1028*; *Ber.*, *1933*, **66**, *1392*), but the values for $E$ and log $PZ$ in nitrobenzene are somewhat lower than his values (*Trans. Faraday Soc.*, in the press).




In the figure our values for log $PZ$ are plotted against $E^{-\frac{1}{2}}$ (compare J., 1937, 538), together with values for hexane and for ethyl alcohol taken from Wassermann. The points for the three polar solvents lie on one straight line, and those for the three non-polar solvents upon a parallel line. For the same activation energy, log $PZ$ is approximately 0·7 greater in the polar solvents. Thus in this respect there is a qualitative similarity between this reaction and the formation of quaternary ammonium salts, *i.e.*, there is a tendency for $E$ to increase in polar solvents, superimposed upon a general correlation between log $PZ$ and $E$.

It is interesting to compare the magnitudes of the effect in the three clear cases where it has been found to exist. For a given activation energy the formation of methylpyridinium iodide occurs about 30 times as fast in the group of highly polar solvents as in the non-polar ones: the formation of allylpyridinium bromide approximately 15 times as fast (Hawkins, J., **1922**, **121**, **1170**; cf. J., **1937**, **544**, Fig. 3), and the addition of benzoquinone to *cyclo*pentadiene approximately 5 times. Thus, although the effect appears in

the Diels–Alder reaction, it is smaller. These results do not decide definitely in favour of either of the mechanisms discussed above. The fact that the influence of polarity appears at all in the Diels–Alder reaction shows that the stabilisation of a polar product cannot be the whole story. Some part of the effect may be due to an actual increase in the collision frequency in the polar solvents. But we may still assume with some probability that the large magnitude of the polar influence in quaternary ammonium salt formation is connected with the stabilisation process.

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THE OLD CHEMISTRY DEPARTMENT,
UNIVERSITY OF OXFORD. [*Received, December 16th, 1937.*]

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# 47. *The Spontaneous Ignition under Pressure of Typical Knocking and Non-knocking Fuels: Heptane, Octane;* iso*Octane, Di*iso*propyl Ether, Acetone, Benzene.*

By M. MACCORMAC and D. T. A. TOWNEND.

SUMMARY.

Previous investigations, which had established a close relationship between ease of spontaneous ignition under pressure and the known knocking propensities in engine practice of the simpler paraffins and olefins, have been extended, and the present paper includes observations with some of the newer 'high-duty' (non-knocking) fuels, notably *iso*octane, di*iso*propyl ether, and acetone.

Much higher pressures are requisite for the spontaneous ignition of side-chain paraffins than for the straight-chain isomers, the temperature ranges in which cool flames are observed and the character of the low-temperature ignition systems induced thereby being much the same in both cases.

The cool-flame zones and the lower-ignition systems of the ethers appear to be composite, and much higher pressures are requisite for the ignition of mixtures of air with di*iso*propyl ether than for those with diethyl ether.

Acetone has been shown to give rise to cool flames and a simple low-temperature system if the observations are extended to sufficiently high pressures; and benzene behaves rather like methane, there being no indication at all of a low-temperature system.

A scheme is suggested whereby the relative knock-rating of a fuel may be assessed from the characteristics of its spontaneous ignition under pressure.

The processes giving rise to the low-temperature ignition systems induced by cool flames are briefly discussed.

IN a recent communication (Kane, Chamberlain, and Townend, J., 1937, 436) earlier observations on the spontaneous ignition under pressure of the paraffin hydrocarbons up to hexar were summarised, and the probable influence of intermediately formed aldehydes i promoting combustion was studied by comparing the ignition-point curves of correspondir paraffins, alcohols, and aldehydes containing up to three carbon atoms; the relationsh between the pressures requisite for spontaneous ignition within a suitable short time la and the critical compression ratios for the occurrence of 'knock' in engine practice was al indicated. In parallel observations on the olefins up to amylene (Kane and Townen *Proc. Roy. Soc.*, 1937, *A*, **160**, 174), it has also been shown that their behaviour is not unli that of the corresponding paraffins, the ignition-point curves exhibiting a sharp fall o narrow critical pressure ranges to a lower system, where at atmospheric pressure only c flames are normally observed; and amylene revealed all the characteristics typical of t higher paraffins. The main difference between the two series, however, lay in the we luminosity and feebleness of the pressure pulses associated with the cool flames of t

olefins, indicating that the processes operative in the low-temperature system are less intense than with the paraffins; moreover, the pre-flame time lags were not only greater but decreased less rapidly with increase in initial pressure. It seemed likely that combustion was promoted in both instances by the formation of the same reactive species, which probably result from the formation of higher aldehydes; and the less vigorous behaviour of the olefins may be attributable either to a slower building up of active centres depending upon aldehyde concentration by virtue of difference in the chemical stages involved, or to the intervention of stronger inhibiting processes. New evidence as to the chemical processes leading to the formation of cool flames and ultimate ignition has recently been forthcoming from the work of Newitt and Thornes (J., 1937, 1656) on propane–oxygen mixtures, a matter of interest being their observation that cool flames seem to depend on the prior formation of a critical concentration of higher aldehydes.

The relationship between ease of ignition under pressure and the knocking propensities of the paraffins up to hexane and the olefins up to amylene seeming conclusive, it became a matter of importance, both from the point of view of their practical application as well as the development of the theory of the combustions concerned, to extend these observations to include *inter alia* some of the newer high-duty fuels, notably side-chain hydrocarbons, ketones, and di*iso*propyl ether. In this paper a brief account and discussion are given of the behaviours of (1) *iso*octane (ββδ-trimethylpentane) in comparison with *n*-heptane and *n*-octane, (2) di*iso*propyl ether, (3) acetone, and (4) benzene. The apparatus and procedure employed were essentially as described by Kane, Chamberlain, and Townend (*loc. cit.*).

*Results.*

1. n-*Heptane,* n-*Octane and* iso*Octane.*—In Fig. 1 curves have been drawn showing the influence of pressure on the ignition points of corresponding weak mixtures with air (0·65 × theoretical concentration of combustible) of *n*-heptane and *n*- and *iso*-octane. The materials employed were all synthetic products supplied by the Eastman Kodak Company having b. p.'s 98—98·5°, 124—126°, and 98—99°, respectively.

The curves for the two normal paraffins (Nos. 1 and 2) are characteristic of those previously determined for propane, butane, pentane, and hexane, there being two pressure minima of ignition in the low-temperature system; moreover, the minimium ignition pressures and temperatures were found to decrease progressively but more slowly as the series was ascended. This is in accord with the observation of Lovell, Campbell, and Boyd (*Ind. Eng. Chem.*, 1934, **26**, 1105) that the tendency to knock of the normal paraffins increases rapidly up to pentane but more slowly thereafter. Moreover, with heptane and octane the time lags (as indicated along the curves) became very short and were not measurable with accuracy; *e.g.*, that for the octane–air mixture was of the order of 0·3 sec. at 350°. In other experiments attempts to determine the ignition-point curve of a corresponding *n*-decane–air mixture had for this reason to be abandoned, for the time lags in the low-temperature range were now less than the interval required for filling the mixture into the explosion vessel.

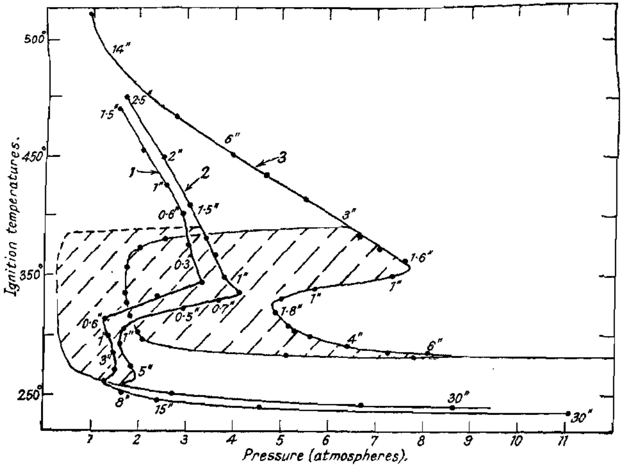
The temperature and pressure limits within which cool flames were observable are defined in the usual way for the heptane–air mixture by the diagonally shaded area; also, owing to the very short time lags, it was possible to determine the upper-temperature boundary only approximately. An interesting feature of the experiments on the paraffin series as a whole was the progressive increase in intensity of the cool flames as the series was ascended, this being marked up to the heptane–air mixtures.

*iso*Octane, the well-known standard for knock-rating, is now produced commercially for blending purposes from *iso*butylene *via* di*iso*butylene (Banks, *J. Inst. Pet. Tech.*, 1937, **23**, 63). Curve No. 3, Fig. 1, relates to a mixture of this material with air corresponding with those of the two normal paraffins (Nos. 1 and 2). As anticipated, the pressures requisite for ignition were much greater than for the *n*-octane–air mixture (No. 1) throughout the whole temperature range, and only one pressure minimum of ignition in the low-temperature system could be located (cf. the behaviour of *n*-butane and *iso*butane; Townend Cohen, and Mandlekar, *Proc. Roy. Soc.*, 1934, *A*, **146**, 126); also at corresponding temperatures the time lags were longer for the side-chain isomer. Although, in general, the char-

acter of the ignitions as well as of the cool flames was much the same with both isomers, yet mixtures with *iso*octane were by far the more sensitive to surface conditions, particularly in the temperature range below 300°.

The influence of pressure on the spontaneous ignition of all the normal paraffins up to octane, as well as of *iso*butane and *iso*octane, having now been studied, there seems little doubt as to the general relationship between the pressures requisite for spontaneous ignition under conditions of appropriate time-lag and temperature and the knock ratings of the fuels concerned, as may be seen from the following figures relating to (*a*) the minimum pressures

Fig. I.




*Corresponding mixtures with air of* (1) n-*octane*; (2) n-*heptane*; (3) iso*octane*.
[*Figures along curves denote time lags* (*seconds*).]

for ignition in the lower system, (*b*) the corresponding time lags, and (*c*) the knock ratings (critical compression ratios) of the paraffins concerned :

| Paraffin. | *A*. Minimum pressure (atm.). | *B*. Time lag (sec.). | *C*. Critical compression ratio (Boyd). | Ratio *A*/*C*. |
|---|---|---|---|---|
| Methane | — | — | (non-knocking) | — |
| Ethane | — | — | 14·0 | — |
| Propane | 6·8 | 3 | 12·0 | 0·57 |
| Butane | 3·2 | 2 | 6·4 | 0·50 |
| Pentane | 2·2 | 1·4 | 3·8 | 0·57 |
| Hexane | 1·9 | 1 | 3·3 | 0·58 |
| Heptane | 1·58 | 0·7 | 2·8 | 0·57 |
| Octane | 1·3 | 0·3 | <2·8 | >0·47 |
| *iso*Butane | 4·8 | 3 | 8·9 | 0·54 |
| *iso*Octane | 4·85 | 1·7 | 7·6 | 0·64 |

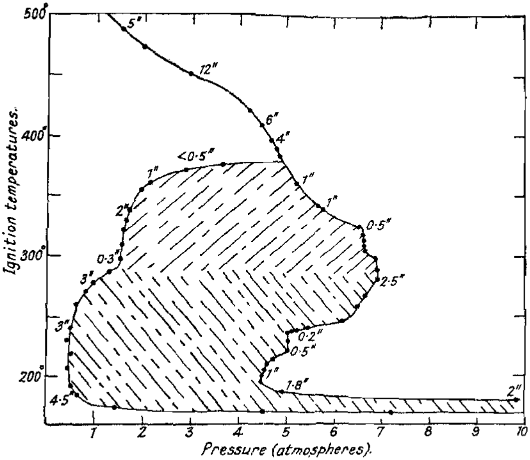
Similar correspondence has also been observed with the olefins (Kane and Townend, *loc. cit.*).

Although the actual numerical consistency of the relationship between the minimum ignition pressures and the critical compression ratios is striking, we would not overstress its importance because (*a*) under engine conditions the minimum pressures would relate to ignition within a time lag not exceeding a few thousandths of a second and it is doubtful

whether the rate of decrease of lag with increase of pressure would conform to the same order with each hydrocarbon, and (*b*) in the case of fuels with critical compression ratios > 6—8 : 1 it seems likely that the compression temperatures would approach 500°, which probably corresponds with the upper ignition range even for very short time lags (cf. Townend and Chamberlain, *Proc. Roy. Soc.*, 1936, *A*, **154**, 108), a matter which is discussed below.

2. *Diisopropyl Ether.*—The use of this ether as an anti-knock fuel for blending purposes has only recently been described (Buc and Aldwin, *J. Soc. Auto. Eng.*, Sept. 1936), and in view of its commercial production from propylene, its potentialities as a fuel are considered to be greater than those of *iso*octane (Banks, *loc. cit.*). We are indebted to Messrs. Trinidad Leaseholds Ltd. for a supply of a good sample of the material, which, after treatment with sodium, was fractionally distilled, the fraction of b. p. 67·4—67·7°/747 mm. being employed for our determinations.

FIG. 2.



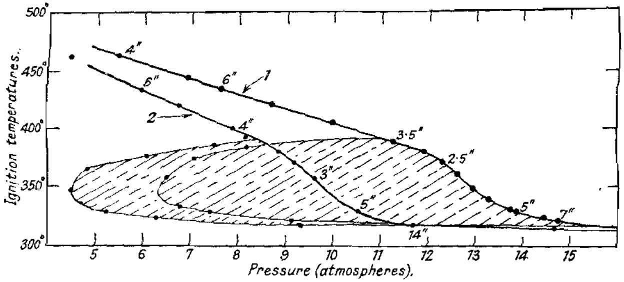

2·5% *Diisopropyl ether–air mixture.*
[*Figures along curves denote time lags (seconds).*]

Fig. 2 shows the ignition-point curve of a 2·5% mixture (theoretical mixture = 2·28%) of this combustible. In general, it resembles that obtained with diethyl ether (Townend and Chamberlain, *Proc. Roy. Soc.*, 1937, *A*, **158**, 415), for the principal lower ignition system was located at much lower temperatures (180—250°) than that usually observed with the paraffin hydrocarbons (240—350°). An interesting feature of the results as a whole, however, was that the cool-flame zone which extended downwards from *ca.* 390° appeared to be composite. Thus a lower cool-flame system giving rise to the principal lower-ignition system extended from *ca.* 170° to 290—300°, the time lags shortening with rise of temperature; at higher temperatures, *viz.*, 300—390°, *i.e.*, in the range where the cool flames of higher paraffins and olefins are found, the lower cool-flame system was replaced by a second system, the time lags increasing abruptly at first and the ignition-point curve in this range being of the type previously observed with the simpler olefins (Kane and Townend, *loc. cit.*). Moreover at pressures above *ca.* 3 atm., experience showed the cool flames to differ somewhat in character, being blue and milder in intensity in the upper system and purple and of

greater intensity in the lower system. Further evidence of the dual character of the lower system with the ether is afforded by the occurrence of minimum time lags for ignition at both *ca.* 240° and 320°; the ignitions below *ca.* 240° following cool flames were also much more violent than those at higher temperatures. It may be recalled that two quite separate cool-flame areas were similarly located in the case of diethyl ether–air mixtures (*idem, ibid.*), although the flames in the upper of these were both green and strong in intensity and more akin to weak ignitions. It appears, therefore, that in the combustion of ethers there is one low-temperature system located at *ca.* 200°, which probably arises as a consequence of a primary oxidation, and another at *ca.* 350°, due to the secondary oxidation of an intermediate product also common to the combustion of higher hydrocarbons (possibly acetaldehyde).

It is also clear from the high pressures requisite to effect ignition over the whole temperature range that di*iso*propyl ether, in contrast to diethyl ether, would be expected to be a non-knocking fuel.

Fig. 3.




*Acetone–air mixtures*: 1 = 5%; 2 = 7·6%.
[*Figures along curves denote time lags (seconds).*]

3. *Acetone.*—Although acetone and other ketones have been frequently reported as being employed as efficient anti-knock fuels, *e.g.*, in the Schneider trophy race (Ricardo, Melchett Lecture to the Institute of Fuel, 1935), yet there do not appear to be any data in the literature regarding their precise knock-ratings. In order to test our general views on the subject, however, we decided to ascertain the characteristics of the ignition under pressure of acetone–air mixtures.

Curves 1 and 2, Fig. 3, show the influence of pressure on the ignition points of two acetone–air mixtures containing 5% (theoretical mixture) and 7·6% of acetone, respectively. The mixtures developed cool flames when high enough pressures were employed, and the ignition-point curves showed a steeper but not marked fall with increase of pressure in the cool-flame temperature range. A feature of the experiments was the high pressures necessary to effect ignition below 400°, and in this respect acetone resembles ethane, although cool flames were not detected with the latter. The cool flames observed with acetone–air mixtures were always very weak; and the pressure pulses associated with them were of an intensity which, when expressed as a percentage of the initial pressure in any particular case, would be related to that developed with other materials discussed in this paper somewhat as follows:

| Acetone. | *iso*Propyl ether. | *iso*Octane. | *n*-Heptane. | *n*-Octane. |
|---|---|---|---|---|
| 1 | Lower 3·5<br>Upper 2·5 | 4·5 | 9 | 10 |

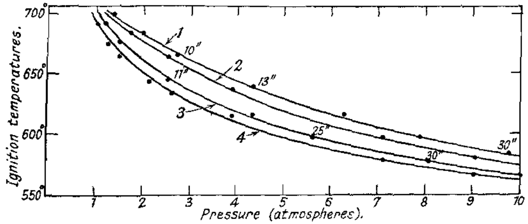
With acetone, however, the cool flames gave rise to a luminescence, lasting up to 10 seconds; this was succeeded by a faint glow which was accompanied by a slow pressure rise,

indicating that the cool-flame reaction was prolonged in the circumstances; the normal ignitions were also weak except at temperatures below 330°.

From the high pressures necessary to effect ignition, acetone would obviously be adjudged a non-knocking fuel.

4. *Benzene–Air Mixtures* (With W. A. P. Fisher).—In the early stages of these investigations some determinations were made of the ignition temperatures of benzene–air mixtures under pressure, this material being the oldest and most commonly employed non-knocking blending fuel. In Fig. 4 ignition-point curves of four mixtures containing 1·36, 2·45, 3·2, and 5% of the combustible (theoretical mixture = 2·7%), curves 1, 2, 3, and 4 respectively, have been drawn. It will be observed that there was never any indication at all of a lower-ignition system, the ignition points falling gradually from about 700° to 560—580° with increase in initial pressure from 1 to about 10 atm.; the time lags were also considerable, increasing from *ca.* 6 to 30 secs. over the same range. The determinations were easily reproducible, and lent strong support to our conviction as to the relationship between the knocking propensities of fuels and their ease of spontaneous ignition under appropriate temperature and pressure conditions.

Fig. 4.



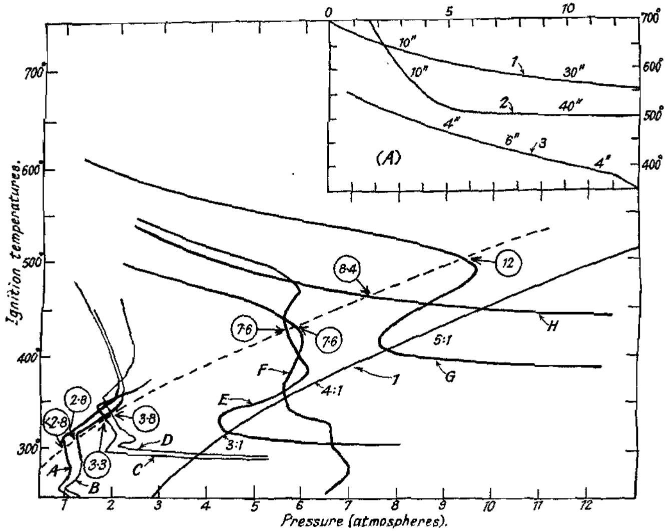

*Benzene–air mixtures*: 1 = 1·36%; 2 = 2·45%; 3 = 3·2%; 4 = 5%.
[*Figures along curves denote time lags (seconds).*]

*The General Relationship between Spontaneous Ignition under Pressure and Knock Ratings.*—So far in these investigations, we have usually compared (as on p. 240) the pressures requisite for spontaneous ignition in the lower system with the critical compression ratios requisite for the incidence of knock in engine practice of the fuels concerned and, having also in mind the observed time lags, we have found this relationship to hold good in a remarkable manner. In order to study the respective behaviours of chemically dissimilar fuels, however, an attempt at a more precise method of comparison is necessary, involving in particular (*a*) ignition-point curves pertaining to ignition within comparable short time lags, and (*b*) a knowledge of the approximate compression temperatures attained by the explosive media at the end of the compression stroke in the cylinder head. Unfortunately, it is impossible with our present method of working to measure very short lags even approaching those comparable with conditions in an engine, so for the present purpose we have plotted in Fig. 5, as far as our results have allowed, curves relating to approximately theoretical mixtures with air of eight representative fuels, indicating where possible the pressures requisite for ignition in a time lag of 1 sec.; with the higher paraffins, where complete curves are not always available, we have marked with a heavy line the portions pertaining to lags of 1 sec. or less. The curves for benzene, methane, and acetone (Inset A), which are non-knocking fuels, are our normal curves relating to the minimum ignition pressures, the lags being of the order of 4 secs. upwards; the pressures would have to be increased appreciably for ignition to occur within 1 sec.

In order to form an opinion of the approximate pressures and temperatures attained on compression by the various explosive media, we have plotted on the same diagram a typical adiabatic curve (No. 1) for compression ratios up to 6 : 1, calculated according to the

relations $T_2 = T_1 \times r^{\gamma - 1}$ and $P_2 = P_1 \times r^{\gamma}$. For simplicity, the value of $\gamma$ has been taken as 1·35, which is generally applicable, and that of $T_1$ as 130°, corresponding approximately with the temperature of the medium before compression at a compression ratio of 4·5.*

FIG. 5.




*One-second lag ignition-point curves: theoretical mixtures with air.*
A = *Octane*, B = *heptane*, C = *hexane*, D = *pentane*, E = isooctane, F = *diisopropyl ether*, G = *propane*, H = *propylene*.
*Values in circles denote known knock ratings.*
*Inset* (A). *Ignition-point curves*: 1 = *Benzene*, 2 = *methane*, 3 = *acetone*.

It being now generally recognised that knock in an engine is conditioned by the chemical reactivity of the unburnt medium ahead of the flame (cf. Egerton *et al.*, *Phil. Trans.*, 1935, *A*, **234**, 433), according to our view, owing to the extreme shortness of the available time interval, any appreciable reaction will be intense, and conditions will proximate to those of the ignition point. Knock will therefore first be expected with any particular fuel when the compression is so increased that the pressure and temperature adiabatically attained approximate to those requisite for spontaneous ignition within an appropriate short time lag. If this be the case, the points of intersection of curve 1 with ignition-point curves pertaining to a lag of (say) 0·005 sec. would indicate approximately the conditions requisite for the incidence of knock. Such ignition-point curves, if determinable, would obviously lie in the direction of higher pressures and to the right of the curves plotted in Fig. 5.† In order to illustrate our interpretation, however, we have

* For more precise data concerning compression temperatures, see Pye, "The Internal Combustion Engine," Oxford University Press, Vol. I, p. 116; Callendar *et al.*, Rep. and Mem., No. 1062, Aeronautical Research Committee, 1926.

† It should be noted that for shorter time lags the actual shift in the direction of higher pressures of the curves shown in Fig. 5 would be much greater for those located at higher than at lower pressures.

shifted curve 1 quite arbitrarily to the left in the direction of lower pressures (dotted curve) so as to intersect the 1-second lag ignition-point curves. It will readily be observed that as so placed the known critical compression ratios, indicated at the points of intersection, all fall into the same order as the pressures requisite for ignition within the same short time lag at an appropriate compression temperature. Such a method should, we think, provide a general means of assessing in the laboratory the relative knock rating of any fuel under preliminary test.

Taking into account all the factors concerned, we regard the treatment just described as the best viewpoint in considering the results as a whole, and although in engine practice other factors, such as dilution with explosion products, the formation of reaction centres before the end of the compression stroke, and the part played by the advancing flame, all call for consideration, there seems little doubt as to their general significance.

A matter of interest also relates to the question whether the formation of a cool flame in the unburnt medium is always a necessary prelude to knock in an engine; and in view of the fact that cool flames have never been observed in our experiments above 410—420° and that this temperature is almost certainly exceeded when compression ratios greater than 6—8 : 1 are employed, we doubt whether such occurrence is essential to the phenomenon, but more probably a critical reaction velocity irrespective of the precise intervening mechanisms which lead to it. This is supported by the fact that, although the iso-lag curves show propane to be more reactive than propylene in the cool-flame temperature range, yet at higher temperatures they cross; and it is significant that the knock rating of propylene is less than that of propane.

*Discussion.*

Although the principal purpose of these investigations has been to substantiate the general relationship between ignition pressures and the knocking propensities of the fuels concerned, yet a main interest still centres upon the correct interpretation of the lower-ignition system and in particular the mechanism of formation of the cool flames which give rise to it. In addition to extending the results already obtained with the lower members of the paraffin series, with both straight and side chains, the experiments described in this paper have (*a*) established the occurrence of two cool-flame regions with ethers, mixtures with di*iso*propyl ether requiring much higher pressures for their ultimate ignition than those with diethyl ether, and (*b*) shown for the first time that, if the behaviour of acetone may be taken as typical, ketones also give rise both to cool flames and to a simple lower-ignition system provided the experiments be extended to sufficiently high pressures.

As far as the paraffins are concerned, the similarity in behaviour of all members containing more than three carbon atoms, in regard to both the location of the cool-flame temperature ranges and the dual pressure minima associated with spontaneous ignition arising therefrom, suggests that the same materials are ultimately concerned in all cases. That higher olefins behave in a manner much the same as that of the higher paraffins also suggests that the substances concerned are intermediate oxidation products common to both combustions and therefore likely to be aldehydes. Also, the fact that acetaldehyde is the simplest aldehyde to show a marked pressure minimum corresponding with that exhibited by all higher hydrocarbons (Kane, Chamberlain, and Townend, *loc. cit.*) indicates the intermediate formation of this material as likely to be a principal factor concerned in the process.

If it be conceded from the work of Edgar and his collaborators (*J. Amer. Chem. Soc.*, 1929, **51**, 1875, 2203) that the oxidation of a higher paraffin involves the formation of the corresponding aldehyde and water at an early stage, then it would appear, as indeed these authors have shown, that the succeeding reactions lead rapidly to the same type of products in all cases; moreover, although little is known concerning the thermal decomposition of higher aldehydes, it would seem not unreasonable, by analogy with the work of Norrish and collaborators on the photolysis of such aldehydes (J., 1935, 1504, etc.), that their thermal decomposition might in part give rise to acetaldehyde and a higher olefin.

No adequate explanation has yet been forthcoming either of the mechanism of, or of the upper temperature limit for, cool flames. Recent experiments carried out by Dr. H. S.

Hsieh in these laboratories on diethyl ether–air mixtures, however, indicate that the mechanisms operative are the same whether the flames are ignited artificially in cold media by means of a hot wire or whether they are developed spontaneously in a sufficiently heated vessel. It would appear, therefore, that there is an upper temperature barrier to the flames which is not exceeded, probably owing to the thermal instability of a chain initiator or material giving rise to a chain initiator, the substances concerned being either stabilised products or possibly free radicals. In this connection, in view of the facts that (i) aldehydes, ethers, and ketones all give rise to cool-flame regions of ignition, (ii) the view is now widely held that the thermal decompositions of these materials proceed by chain processes involving free radicals (cf. Rice and Rice, "The Aliphatic Free Radicals," Johns Hopkins Press, 1934), and (iii) that the presence of oxygen may provide reaction centres accelerating the decompositions (cf. Letort, *Compt. rend.*, 1933, **197**, 1042), it seems not unlikely that their thermal stability may be a factor influencing the low-temperature phenomena. Moreover, the probable interplay of per-acids and peroxides is also as yet not entirely understood.

Among recent theories of the processes involved, von Elbe and Lewis (*J. Amer. Chem. Soc.*, 1937, **59**, 976) have suggested, with regard to the combustion of higher paraffins, the formation of alkyl peroxide radicals of short life as giving rise to multiple branching in the low-temperature range by condensation with an aldehyde, and further oxidation of the product to yield hydroxyl radicals. With higher aldehydes a similar process is presumably involved, the radical concerned being of the type R·CO(OO); and in both cases cool flames are regarded as arising by stepwise degraded oxidation of R·CO radicals (produced from aldehydes) to $CH_3$·CO, which is further oxidised to energised formaldehyde, the spectrum of which is characteristic of the emission from cool flames. Although such an explanation shows a possible cause of the low-temperature systems with aliphatic hydrocarbons and higher aldehydes, yet it seems doubtful whether it can be adapted to meet the case of (say) acetone and possibly the ethers.

The authors thank the Gas Light and Coke Company for their Research Fellowship (M.M.), during the tenure of which the investigation has been carried out, and also Mr. W. A. P. Fisher, B.A., for carrying out the determinations with benzene–air mixtures.

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## 48. *Kinetics of the Catalysed Polymerisation of Styrene. Part I. Experimental Methods and Some General Features of Stannic Chloride Catalysis.*

By GWYN WILLIAMS.

The polymerisation of styrene, catalysed by pure stannic chloride, has been examined in carbon tetrachloride solution at 25—45°. The process can be followed by quantitative bromination of the residual monomer present in a polymerising mixture. The styrene disappearing during polymerisation is shown, by quantitative precipitation of the polymer, to be equivalent to the polystyrene formed (mean molecular weight 1200—2700). Both polymer size, which usually remains constant through the course of a given reaction, and polymerisation rate are more sensitive to change in concentration of styrene than of catalyst. The reactions have induction periods and, over a three-fold concentration range, the maximum rate is approximately proportional to the concentration of catalyst. The rate of polymerisation is reproducible with freshly distilled styrene and is not affected by the addition of benzoyl peroxide. The polymerisation of styrene, which has been kept for some time and contains peroxides, is retarded in its early stages.

THE thermal polymerisation of styrene is influenced by oxygen (Staudinger an Lautenschläger, *Annalen*, 1931, **488**, 1), and significant kinetic results for uncatalyse polymerisation are obtainable only with rigid exclusion of oxygen (Breitenbach an

Rudorfer, *Monatsh.*, 1937, **70**, 37; Dostal and Jorde, *Z. physikal. Chem.*, 1937, *A*, **179**, 23; Suess, Pilch, and Rudorfer, *ibid.*, p. 361; Schulz and Husemann, *ibid.*, 1937, *B*, **36**, 184). In the presence of a powerful polymerisation catalyst, such as stannic chloride, the influence of oxygen should have less importance, particularly since it is possible to study the catalysed polymerisation at temperatures at which the spontaneous polymerisation of styrene is very slow, with or without a solvent.

With anhydrous stannic chloride as catalyst, styrene polymerises in carbon tetrachloride or chloroform solution at a rate measurable at room temperature, giving hemi-colloidal products with an average molecular weight of the order 3,000 (Staudinger, "Die Hochmolekularen Organischen Verbindungen," Berlin, 1932, p. 159). Polymerisation may be preceded by periods of initial inhibition (Williams, *Nature*, 1937, **140**, 363), but, with pure materials, these are absent. The purpose of this paper is to define conditions affecting the consistency of kinetic results, and to describe certain characteristics of the stannic chloride polymerisation of styrene. Inhibition phenomena and detailed kinetics will be considered in later papers.

Styrene may be estimated by quantitative bromination of the double bond. Since it can be established that the styrene disappearing during polymerisation is equivalent to the polymer formed, bromination analysis for residual monomeric styrene provides a convenient method for following the progress of polymerisation. It is of particular advantage for catalysed polymerisation, because the presence of stannic chloride in the system would require the modification of methods depending on isolating and weighing the polymers, either by distilling off solvent and residual monomer (Mark and Raff, *Z. physikal. Chem.*, 1936, *B*, **31**, 275) or by precipitating the polymer in methyl alcohol (Schulz and Husemann, *ibid.*, **34**, 187). The objection in the latter case is that, with stannic chloride, under certain conditions, part of the polystyrene produced is of low enough molecular weight to be soluble in methyl alcohol.

We find that the method of bromination analysis can also be used to follow the polymerisation of vinyl acetate; and Hammick and Langrish (J., 1937, 797) have applied a similar procedure to the polymerisation of indene and *cyclo*pentadiene.

## EXPERIMENTAL.

*Materials.*—Styrene, made from cinnamic acid, and containing originally a quinol inhibitor, was repeatedly distilled (through a column) under nitrogen at 5—10 mm. pressure. Comparison experiments were made with commercial styrene, specially purified by low-pressure fractionation through the kindness of Dr. K. C. D. Hickman.

Carbon tetrachloride, "Eastman, free from sulphur," was washed, dried, and distilled through a fractionating column before use as solvent.

Stannic chloride was purified essentially as described by Briscoe (J., 1915, **107**, 63) and by Baxter and Starkweather (*J. Amer. Chem. Soc.*, 1920, **42**, 905). The anhydrous substance ("c.p. analysed") was distilled in a sealed, evacuated, Pyrex-glass apparatus, which had been previously heated in a flame at a pressure of $10^{-5}$ mm. After two distillations at room temperature, the substance was distilled twice by evaporation at $-20°$ into receivers cooled with liquid air. A first fraction was each time collected separately in liquid air, to remove hydrogen chloride, and a residuum was left in the distilling vessel. Finally, the stannic chloride was collected in a U-tube, from which known volumes were evaporated into small bulbs of thin glass, cooled with liquid air. These were sealed off one by one, and weighed. The final specimens were free from any trace of the solid fragments, present in commercial stannic chloride, which survived the earlier distillation stages.

*Estimation of Styrene.*—The styrene solution in carbon tetrachloride is run into a standard solution of bromine in glacial acetic acid. Addition to the double bond takes place at once, and the excess of bromine is destroyed with potassium iodide, the liberated iodine being titrated with sodium thiosulphate. Table I illustrates the accuracy of the analysis and shows that the method is still valid when polystyrene and stannic chloride are present in the solution. Stannic chloride appears to catalyse a slow bromine attack on the polymer, but this does not spoil the analysis, provided that the bromine excess be destroyed without delay.

*Rate Measurements.*—Polymerisation was started by crushing a weighed glass bulb, containing stannic chloride, under the surface of a standard solution of styrene in carbon

TABLE I.

| Styrene concn., mols./l. | | Ratio | | $(C_8H_8)_n$ concn., as |
|---|---|---|---|---|
| Calc. | Found.* | $Br_2/C_8H_8$. | $SnCl_4$, mols./l. | mols. of $C_8H_8$/l. |
| 1·733 | 1·735 (3; 0·15%) | 1·4 | — | — |
| 1·733 | 1·738 | 1·4 | 0·04 | 0·1 |
| 1·724 | 1·721 | 1·3 | — | — |
| 0·866 | 0·867 (5; 0·14%) | 1·4 | — | — |
| 0·866 | 0·866 | 1·5 | — | 1·0 |
| 0·866 | 0·860 | 1·5 | 0·05 | 0·5 |
| 0·432 | 0·431 (4; 0·3%) | 1·1 | — | — |
| 0·432 | 0·430 | 1·1 | — | 0·1 |
| 0·432 | 0·432 | 1·1 | 0·03 | 0·1 |
| 0·174 † | 0·175 (2) | 1·8 | — | — |
| 0·0867 | 0·0866 (3; 0·2%) | 1·6 | — | — |

* The figures in parentheses represent the number of individual measurements and the mean deviation from the mean.

† In chloroform solution.

tetrachloride. The reaction vessels were 100 c.c. or 50 c.c. standard flasks or stoppered bottles of brown glass. 2-C.c. portions of the reaction mixture (kept in a thermostat) were extracted at intervals and analysed for monomeric styrene by the bromination method. At the end of the experiment, the crushed glass in the reaction vessel was filtered off and weighed, in order to determine the amount of stannic chloride introduced.

*Molecular-weight Measurements.*—Portions of the polymerising mixture were also removed at intervals and diluted to a known volume in carbon tetrachloride. The polystyrene content at the moment of extraction was found from the reaction curve, and the mean molecular weight of the polymer was determined by viscosity measurements on the diluted solutions, an Ostwald viscometer being used at 25°. The polystyrene content of the diluted extracts did not alter during the viscosity measurements; the dilution applied (at least ten-fold) reduced the polymerisation rate to negligible proportions. The dissolved stannic chloride did not affect the viscosity of carbon tetrachloride (*e.g.*, viscometer flow-times for pure solvent and for 0·065M-$SnCl_4$ in the solvent were 353·8 and 353·9 secs., respectively). The polystyrene dilution was chosen so as to give an increment of 15—40 secs. in the flow-time over that for pure carbon tetrachloride, but the concentrations were always well below the upper limits recommended by Schulz (*Z. Elektrochem.*, 1937, **43**, 479). The solutions were filtered when necessary.

The results thus obtained from solutions made up directly from the reaction mixture were checked occasionally by measurements made with solutions of dry polystyrene, isolated from the reaction mixture by precipitation in methyl alcohol (*e.g.*, $\eta_{sp.}/c$ values for solution made from isolated polystyrene and for diluted reaction mixture were 0·876 and 0·887 respectively).

*Results.*—*Course of the reaction.* In order to determine whether the loss of monomeric styrene during polymerisation was fully accounted for by the formation of polystyrene of high molecular weight, 10-c.c. portions of reaction mixture were run into pure methyl alcohol. The precipitated polystyrene was filtered off through porous porcelain, washed with dilute hydrochloric acid and methyl alcohol, and dried to constant weight at 100°. Table II contains results for several reaction mixtures, made up from different lots of styrene and catalyst, with various rates of polymerisation.

The fall in concentration of monomeric styrene is evidently equivalent to the increase in concentration of high molecular weight polystyrene. With lower initial styrene concentrations, part of the polystyrene formed is soluble in methyl alcohol (cf. Staudinger *et al.*, *Ber.*, 1929, **62**, 260), and a further yield of polystyrene can be obtained by adding water to the methyl alcohol filtrate. It is thus possible to state that, with low initial styrene concentrations, polymers with molecular weights below 1000 (Staudinger, *op. cit.*, p. 161) are formed in appreciable amount. These are absent at higher styrene concentrations, as indicated in Table II.

*Chain-length of polymeric product.* The results of viscosity measurements are given in Tables III and IV. The immediate application of Staudinger's law to these viscosity results presents certain difficulties. They arise from three causes, now discussed. Staudinger's viscosity law is generally used in the form

$$\eta_{sp.}/c = K_m \cdot M \quad \quad (1)$$

TABLE II.

*Quantitative precipitation of polymerised product.*

| Expt. No. | Temp. | Initial $C_8H_8$, mols./l. | $SnCl_4$, M. | Time, hrs. | Polymer found, g. | Mol. wt. | % Polymerisation. By $Br_2$ titrn. | By wt. of polymer. |
|---|---|---|---|---|---|---|---|---|
| 67 | 25° | 1·730 | 0·0571 | 0·59 | 0·258 | — | 16·9 | 14·3 |
| 66 | 25 | 2·110 | 0·0139 | 1·26 | 0·407 | — | 18·6 | 18·6 |
| 37 | 25 | 1·710 | 0·0644 | 1·68 | 0·423 | 2470 | 26·3 | 23·8 |
| 23 | 25 | 1·734 | 0·1258 | 23·3 | 0·738 | — | 39·1 | 40·8 |
| 35 | 25 | 1·686 | 0·0950 | 1·70 | 0·691 | 2740 | 40·6 | 39·5 |
| 54 | 35 | 1·743 | 0·0641 | 1·43 | {0·980, 0·082*} | 2240 | 59·1 | 58·6 |
| 36 | 25 | 1·72 | 0·0644 | 2·75 | 1·072 | 1790 | 62·8 | 60·1 |
| 38 | 25 | 1·710 | 0·0870 | 19·2 | 1·493 | 2890 | 80·5 | 83·6 |
| 43 | 25 | 0·866 | 0·1090 | 8·63 | 0·363 | 2730 | 46·4 | (40·2) * |

* Some polymer, soluble in methyl alcohol, precipitated in water. Water precipitate not recovered in No. 43.

where $\eta_{sp.}$ = specific viscosity = $[\eta(\text{soln.}) - \eta(\text{solvent})]/\eta(\text{solvent})$, $c$ = polymer concentration (as mols. of $C_8H_8$/l.), and $K_m$ = a constant for a given polymer-homologous series. $K_m$ will not have the value appropriate to a set of individually uniform homologous polymers, because (*a*) branching of the polystyrene chain, which occurs in high-temperature polymerisation (Staudinger and Schulz, *Ber.*, 1935, **68**, 2320; Signer, *Helv. Chim. Acta*, 1936, **19**, 897), is not known to be excluded in catalytic polymerisation; (*b*) $K_m$ for polystyrenes increases steadily as the molecular weight falls below 5,000 (Staudinger, *op. cit.*, p. 179); (*c*) we are dealing with unfractionated polymer mixtures (cf. Schulz, *Z. physikal. Chem.*, 1935, *B*, **30**, 393; 1936, *B*, **32**, 27).

It seems best, therefore, to lay emphasis on the values for $\eta_{sp.}/c$ in the tables, rather than on any molecular weights calculated from them. An estimate of the average degree of polymerisation ($n$ in tables) has been calculated from the following equation (Staudinger, *op. cit.*, p. 181; *Z. Elektrochem.*, 1934, **40**, 434):

$$\eta_{sp.}/c = an + b \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $a$ and $b$ represent, respectively, the contributions of the chain carbon atoms and of the end-groups to the viscosity; $b$ is taken as 0·2 (Staudinger, *op. cit.*) and $a$ as $2{\cdot}5 \times 10^{-2}$, being the mean of six values determined by Staudinger for unfractionated polymers, having cryoscopic molecular weights between 2,500 and 4,900. Equation (2) then gives values of $n$ for our polymers which are in reasonable accord with Staudinger's cryoscopic values for unfractionated mixtures with corresponding $\eta_{sp.}/c$. No reliance can be placed on the absolute values of $n$ given in the tables, but their variation may have significance.

It appears from Table III that, within experimental error, the average molecular weight of the polymer formed is the same at all stages of the reaction. Constancy of polymer size during polymerisation has been observed in the non-catalytic polymerisation of styrene without a solvent (Staudinger and Frost, *Ber.*, 1935, **68**, 2351; Schulz and Husemann, *loc. cit.*), and a similar result is referred to by Flory (*J. Amer. Chem. Soc.*, 1937, **59**, 241) for the (probably catalytic) polymerisation of methyl methacrylate. On the other hand, Schulz and Husemann consider that, when a solvent is present, polymer size should fall during the reaction. A tendency in this direction is visible in Expt. 54/55 in Table III.

Table IV(*a*) emphasises that the initial styrene concentration is a dominant factor in determining polymer size, a four-fold change of styrene concentration being sufficient to produce a far more noticeable effect on polymer size than changes in the other possible variables shown in Table IV(*b*) and IV(*c*). In fact, although it is an established feature of polymerisation processes that rise of temperature and increase in the concentration of a catalyst both tend to lower the molecular weight of the polymer product (cf., *e.g.*, Staudinger, *op. cit.*, pp. 159, 339), the range of experimental conditions shown in Table IV(*b*) and IV(*c*) is not wide enough to bring out any systematic change of polymer size with either of these variables. The results in Table IV(*c*) are for experiments in which polymerisation was preceded by periods of total inhibition (*Nature*, 1937, **140**, 363), probably caused by the presence of hydrogen chloride in the stannic chloride catalyst.

TABLE III.

*Variation of polymer size with extent of polymerisation.*

| Expt. No. | Temp. | Initial $C_8H_8$, M. | $SnCl_4$, M. | Polymerisation, %. | $\eta_{sp.}/c$. | *n*. |
|---|---|---|---|---|---|---|
| 48 | 25° | 1·73 | 0·0507 | 29·5 | 0·769 | 23 |
| | | | | 43·9 | 0·767 | 23 |
| | | | | 54·3 | 0·826 | 25 |
| | | | | 65·9 | 0·765 | 23 |
| | | | | 76·9 | 0·728 | 21 |
| | | | | 96·6 | 0·689 | 20 |
| 49 | 35 | 1·743 | 0·0763 | 29·7 | 0·753 | 22 |
| | | | | 62·8 | 0·825 | 25 |
| | | | | 81·8 | 0·702 | 20 |
| 54/55 | 35 | 1·743 | 0·0641 | 24·3 | 0·914 | 29 |
| | | | | 45·4 | 0·836 | 25 |
| | | | | 67·1 | 0·818 | 25 |
| | | | | 81·6 | 0·761 | 22 |
| 51 | 45 | 1·753 | 0·0450 | 14·1 | 0·706 | 20 |
| | | | | 37·7 | 0·900 | 28 |
| | | | | 68·6 | 0·813 | 25 |
| 46 | 25 | 0·866 | 0·0507 | 29·8 | 0·620 | 17 |
| | | | | 40·8 | 0·565 | 15 |
| | | | | 91·3 | 0·622 | 17 |
| 50 | 35 | 0·880 | 0·0560 | 11·8 | 0·514 | 13 |
| | | | | 17·0 | 0·525 | 13 |
| | | | | 36·3 | 0·500 | 12 |
| | | | | 48·0 | 0·554 | 14 |
| | | | | 58·2 | 0·539 | 14 |

TABLE IV.

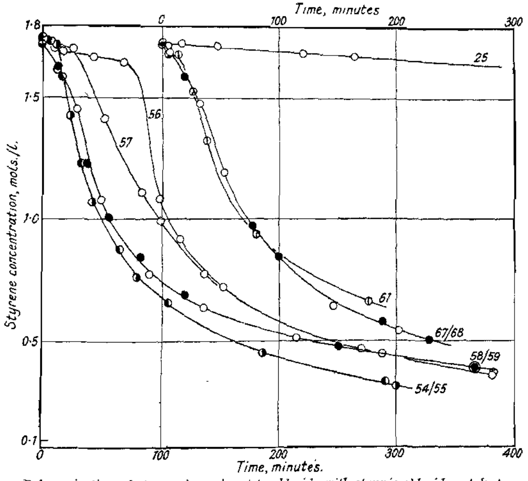
| Expt. No. | Temp. | Initial $C_8H_8$, mols./l. | $SnCl_4$, *s*, mols./l. | $\eta_{sp.}/c$. | *n*. | Maximum rate,* $r_m$, min.$^{-1}$. | $r_m/s$. |
|---|---|---|---|---|---|---|---|
| | | (*a*) Dependence of polymer-size on initial styrene concentration. | | | | | |
| 50 | 35° | 0·880 | 0·0560 | 0·526 | 13 | — | — |
| 49 | 35 | 1·743 | 0·0763 | 0·760 | 22 | — | — |
| 54/55 | 35 | 1·743 | 0·0641 | (0·827) | (25) | — | — |
| 47 | 25 | 0·433 | 0·0507 | 0·507 | 12 † | 0·00010 | 0·002 |
| 46 | 25 | 0·866 | 0·0507 | 0·602 | 16 | 0·0019 | 0·037 |
| 48 | 25 | 1·730 | 0·0507 | 0·757 | 22 | 0·0315 | 0·62 |
| | | (*b*) Variation of catalyst concentration. | | | | | |
| 66 | 25 | 2·110 | 0·0139 | — | — | 0·012 | 0·86 |
| 39 | 25 | 1·724 | 0·0791 | 0·691 | 20 | — | — |
| 42 | 25 | 1·697 | 0·0715 | 0·755 | 22 | — | — |
| 36 | 25 | 1·736 | 0·0644 | 0·860 | 26 | 0·042 | 0·65 |
| 37 | 25 | 1·714 | 0·0644 | 0·817 | 25 | — | — |
| 58 | 25 | 1·732 | 0·0422 | 0·758 | 22 } | 0·027 | 0·64 |
| 59 | 25 | 1·732 | 0·0422 | 0·831 | 25 } | | |
| 56 | 25 | 1·732 | 0·0422 | 0·744 | 22 | — | — |
| 57 | 25 | 1·732 | 0·0422 | 0·738 | 22 | — | — |
| 44 | 25 | 0·870 | 0·0560 | (0·690) | (20) | 0·0016 | 0·029 |
| 43 | 25 | 0·866 | 0·109 | (0·64) | (18) | 0·0026 | 0·024 |
| 45 | 25 | 0·860 | 0·150 | 0·603 | 16 | 0·0048 | 0·032 |
| 30 | 25 | 0·850 | 0·0939 | 0·631 | 17 | | |
| 29 | 25 | 0·855 | 0·114 | 0·645 | 18 | | |
| 51 | 45 | 1·753 | 0·0450 | 0·806 | 24 | | |
| 52 | 45 | 1·753 | 0·0816 | 0·755 | 22 | | |
| 53 | 45 | 1·753 | 0·0816 | 0·769 | 23 | | |
| | | (*c*) Experiments with initial inhibition. | | | | | |
| 7 | 25 | 1·724 | 0·0133 | { 0·792 | 24 at 29·3% polymn. | | |
| | | | | { 0·819 | 25 at 92·0% polymn. | | |
| 10 | 25 | 1·74 | 0·0894 | 0·824 | 25 | | |
| 9 | 25 | 1·75 | 0·157 | 0·887 | 27 | | |
| 11 | 25 | 1·734 | 0·193 | 0·772 | 23 | | |

* The maximum rate of polymerisation is expressed as mols. per litre of styrene disappearing p minute.

† In Expts. 47, 46, 48, *n* is approximately proportional to the square root of the styrene concentrati (cf. Schulz and Husemann, *Z. physikal. Chem.*, 1937, *B*, **36**, 193).

DISCUSSION.

*The Rate of Polymerisation.—Effect of peroxides.* The rate of polymerisation is measured at temperatures (25—45°) at which the spontaneous polymerisation of styrene is negligibly slow even in the presence of oxygen (*cf.* Staudinger and Lautenschläger, *loc. cit.*). It follows that oxygen can only influence the reaction by acting on polymerisation chains which have already been started by the stannic chloride catalyst. The styrene used for polymerisation experiments was tested for the presence of peroxides by shaking with sodium thiocyanate solution and ferrous ammonium sulphate (Kharasch and Mayo, *J. Amer. Chem. Soc.*, 1933, **55**, 2468). Freshly distilled styrene gave no response, but a detectable peroxide content developed in styrene after a few days' keeping at room temperature. In order to test the influence of peroxide content on the rate of polymerisation, benzoyl peroxide was added to certain reaction mixtures. Results are




*Polymerisation of styrene in carbon tetrachloride with stannic chloride catalyst. Curves 25, 61, and 67/68 are on the upper time scale. Data for the curves are given in Table IV.*

shown in the diagram, which illustrates ten experiments. On curves 58/59 and 67/68, the black circles represent reaction mixtures containing 0·01M- and 0·02M-benzoyl peroxide respectively. The white circles on the same curves are for identical reaction mixtures without peroxide. Added peroxide has thus no detectable effect with freshly distilled styrene at 25°. On the other hand, styrene which had been kept in a stoppered bottle for 18 days after distillation gave a positive reaction to the peroxide test; its polymerisation was slow in the initial stages (compare curve 57 with curve 58/59). Slow initial polymerisation rates were often observed with "aged" styrene (*e.g.*, curve 56). An extreme example is illustrated by curve 25, which shows the initial stages of polymerisation for some styrene which had been kept for 3½ months; polymerisation proceeded in approximately zero-order reaction to 60% completion in 73½ hours.

Polymerisation of styrene without an added catalyst is said to be faster in "aged" styrene than in fresh styrene (Stobbe and Posnjak, *Annalen*, 1909, **371**, 259; Stobbe,

*ibid.*, 1915, **409**, 1). This acceleration is almost certainly due to the catalytic effect of peroxides formed by the autoxidation of styrene (cf. Cuthbertson, Gee, and Rideal, *Nature*, 1937, **140**, 889), since an anti-oxidant, such as quinol, stabilises styrene against spontaneous polymerisation at room temperature, and does not influence polymerisation in the absence of oxygen at 100° (Suess, Pilch, and Rudorfer, *loc. cit.*). The retardation of polymerisation in "aged" styrene may be due to the inhibiting action of an autoxidation product, which is allowed full play owing to the catalytic inactivity of peroxides towards the polymerisation of styrene at 25° in the presence of stannic chloride. The mechanism of this "ageing" effect is, however, a matter for further experiment. "Ageing" does not seem seriously to alter the molecular weight of the polymerisation product. Thus, the polystyrene from reaction 25 gave $\eta_{sp.}/c = 0{\cdot}87$ ($n = 27$), which may be compared with the data in Table IV for other reaction mixtures with 1·73M. initial styrene concentration. In general, polymer size seems to be less influenced by adventitious circumstances than is the rate of polymerisation.

*Reproducibility of rate measurements.* The reaction is not sensitive to casual surface influences, as are some polymerisations (Breitenbach and Raff, *Ber.*, 1936, **69**, 1107); curve 54/55 is for a reaction mixture which was divided into two parts immediately after mixing. Polymerisation was followed in the two parts separately, one being in a standard flask and one in a bottle of amber glass. To secure comparable conditions for a series of experiments at varying styrene concentrations, appropriate quantities of a freshly made stannic chloride solution were added as quickly as possible to solutions of freshly distilled styrene. The reproducibility obtainable under these conditions is illustrated by curve 58/59, which represents two reaction mixtures made up in this way. Curve 61 and curve 67/68 represent entirely independent reaction mixtures made up to approximately the same concentrations with different styrene solutions and two separate stannic chloride bulbs (see p. 247). Curve 67/68, like curve 54/55, represents two mixtures examined separately, but obtained by division of an original mixture into two parts.

*Maximum rate.* As may be seen from the diagram, the reaction shows an induction period.* A typical experiment is given in full below.

Expt. 48. Styrene = 1·730M. $SnCl_4$ = 0·0507M. Temp. 25° ± 0·02°.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Time (mins.) | 0 | 6·20 | 19·60 | 33·10 | 45·0 | 67·7 | 86·2 |
| Styrene concn. (M) | 1·730 | 1·689 | 1·651 | 1·298 | 1·106 | 0·926 | 0·836 |
| Polymerisation, % | — | 2·37 | 4·57 | 25·0 | 36·1 | 46·5 | 51·6 |
| Time (mins.) | 153·0 | 245 | 388 | 516 | 900 | (6 days) | |
| Styrene concn. (M) | 0·640 | 0·513 | 0·391 | 0·334 | 0·221 | 0·062 | |
| Polymerisation, % | 63·0 | 70·4 | 77·4 | 80·6 | 87·2 | 96·5 | |

In this particular experiment, the maximum rate of disappearance of styrene (0·03] mol./l./min.) is reached at the stage of 9·3% polymerisation. In a series of comparab experiments with fresh styrene (see Table IV), the maximum rate $r_m$ is found (with rather narrow concentration limits) to be approximately proportional to the concentratic of stannic chloride for a given initial concentration of styrene. It increases enormous as the initial styrene concentration is raised. A wider variation of the reacta concentrations is required before definitive conclusions can be reached.

A curious feature in certain experiments is the appearance of a short prelimina stage of *decreasing* velocity, succeeded by the induction period leading to the ma reaction (*e.g.*, curve 56). The significance of this preliminary stage has not yet be determined. It may, perhaps, be due to an independent reaction forming a distyrer which plays no part in the growth of long polymer chains (cf. Risi and Gauvin, *Canadi J. Res.*, 1936, *B*, **14**, 255), and which is detectable only at the very beginning of t reaction, before the long-chain polymerisation has got fairly under way.

*Conclusion.*—The reaction kinetics and the form of the polymerisation curves will discussed in a later paper. If we adopt the chain theory of polymerisation process which has been considered recently by a number of authors, the stannic chloride catal may play a part (*a*) in the initiation of polymerisation chains (probably by forming

* To be distinguished from the *inhibition* periods referred to previously (*Nature*, 1937, **140**, 363

complex with monomeric styrene), (*b*) in the growth of chains, (*c*) in breaking the chains. The results given in this paper indicate that the following features may be characteristic of the stannic chloride catalysis of styrene polymerisation in solution: (1) greater sensitiveness of polymer size and polymerisation rate to changes of styrene concentration than to changes of catalyst concentration, (2) approximate proportionality between maximum polymerisation rate and catalyst concentration, (3) relative constancy of polymer size through the whole course of a given reaction. If these results can be substantiated over a wider range of conditions, the simplest interpretation may prove to be that the principal function of the catalyst lies in the chain-initiation stage. If the catalyst influences stage (*b*), it must also participate in stage (*c*).

The results given in Table IV for different temperatures are not for comparable specimens of styrene and are therefore unsuitable for calculations of activation energy.

My thanks are due to Dr. S. E. Sheppard for his encouraging interest in this work, and to Messrs. R. H. Wagner and F. H. Horn, of this laboratory, for assistance with the viscosity measurements.

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Rochester, New York. [*Received, December 17th*, 1937.]

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## 49. *Studies on Vitamin E. Part III. Observations on the Structure of α- and β-Tocopherol.*

By F. Bergel, A. R. Todd, and T. S. Work.

β-Tocopherol, isolated as its allophanate from wheat germ oil (Part II, *Biochem. J.*, 1937, **31**, 2257) and showing full vitamin E activity in a dosage of 5 mg., is probably identical with the cumotocopherol of John (*Z. physiol. Chem.*, 1937, **250**, 11) and the neotocopherol of Karrer, Salomon, and Fritzsche (*Helv. Chim. Acta*, 1937, **20**, 1422); the name "β-tocopherol" is retained. α-Tocopheryl allophanate is obtained in varying amounts along with β-tocopheryl allophanate from the same sample of wheat germ oil. Pyrolysis of vitamin E concentrates from wheat germ oil gives mixtures of duroquinol and ψ-cumoquinol. Pure β-tocopherol yields on pyrolysis ψ-cumoquinol, accompanied by a small amount of a quinol of higher m. p. Synthetic *cetyl* and *allyl* ethers of duroquinol differ markedly from the tocopherols in absorption spectrum and reducing properties. The possibility that the tocopherols may be chroman or coumaran derivatives is under investigation.

In Part II (*loc. cit.*) we described the isolation of a crystalline optically active allophanate, m. p. 143·5—144·5°, from the unsaponifiable matter of wheat germ oil. This substance yielded on hydrolysis an oil, β-tocopherol, of approximate formula $C_{29}H_{50}O_2$, which showed full vitamin E activity in rats in a dosage of 5 mg. John (*loc. cit.*) and Karrer, Salomon, and Fritzsche (*loc. cit.*) have independently isolated in similar fashion allophanates, m. p. 146° and 143—144°, respectively, which from their physical and chemical properties are almost certainly identical with our compound.

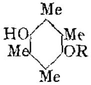
John describes the parent alcohol of his substance as cumotocopherol, and the Swiss workers use the name neotocopherol. We prefer to retain the term β-tocopherol which Evans, Emerson, and Emerson (*J. Biol. Chem.*, 1936, **113**, 319) introduced, since the β-tocopheryl allophanate they described had m. p. 138°, this being the normal m. p. of our crude β-tocopheryl allophanate. The main impurity in this material, m. p. 138°, appears to be a little β-amyrin allophanate, m. p. 273—275°; its removal is a matter of considerable difficulty and is accompanied by a loss of material. The introduction of entirely new names to describe a substance which is almost certainly only a purer specimen of one already in the literature seems to us undesirable. John (*loc. cit.*) states that his tocopherol was active in a minimum dosage of 8 mg., whereas we have had partial activity in dosages as low as 3 mg.; Karrer and his collaborators (*loc. cit.*) give no values for biological activity. This disagreement with regard to biological activity is probably of little significance,

however, as such differences are almost certain to arise where no standardised biological test method is available.

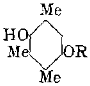
In Part II (*loc. cit.*) we reported that only traces of an allophanate corresponding to the α-tocopheryl allophanate of Evans, Emerson, and Emerson (*loc. cit.*) were obtained. This result we were at first inclined to attribute to a difference between our starting material and that of the American workers, but we have since isolated varying amounts of this compound as well as β-tocopheryl allophanate in different isolations from the same batch of wheat germ oil concentrate. This is the more remarkable as our isolation method has been apparently identical in all cases.

This unaccountable variation in the yield of α-tocopheryl allophanate suggests the possibility that it may be an artefact. The properties and analytical values of our α-tocopheryl allophanate are in agreement with those given by Evans, Emerson, and Emerson (*loc. cit.*) and we confirm their observation of its optical inactivity. The suggestion of Drummond and Hoover (*Biochem. J.*, 1937, **31**, 1852) that β-tocopherol is formed from the α-compound during the isolation process seems unlikely in view of the optical activity of β-tocopheryl allophanate. The total amount of α-tocopheryl allophanate which has been available to us is small, so we have been unable to examine it very closely.

In early experiments (Todd, Bergel, Waldmann, and Work, *Nature*, 1937, **140**, 361) we found, in accordance with Fernholz's results (*J. Amer. Chem. Soc.*, 1937, **59**, 1154), that highly active vitamin E concentrates from rice and wheat germ oils gave duroquinol on heating to about 360°; moreover, concentrates yielding no duroquinol had no biological activity. It was observed, however, that the crude crystalline distillate obtained on pyrolysis generally had a m. p. considerably below 200° and that reasonably pure duroquinol could only be obtained from it after several recrystallisations. Further work on wheat oils showed that this low m. p. was due to the presence in the distillate of varying amounts of a second quinol, m. p. 165—166°, giving on oxidation a steam-volatile quinone, m. p. 28—30°. When slightly impure β-tocopherol was used, this lower-melting quinol was the main product, although some duroquinol was also formed. While these experiments were in progress John (*loc. cit.*) announced that "cumotocopherol" gave ψ-cumoquinol (II; R = H), m. p. 165—170°, on pyrolysis and that it must be an ether of this quinol of possible formula (II; R = $C_{19}H_{37}$) and α-tocopherol correspondingly (I; R = $C_{19}H_{37}$), *i.e.*, that the two compounds were homologues. Our quinol, m. p. 165—166°, we identified by analysis and direct comparison with synthetic ψ-cumoquinol.



(I.)



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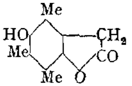


(III.)

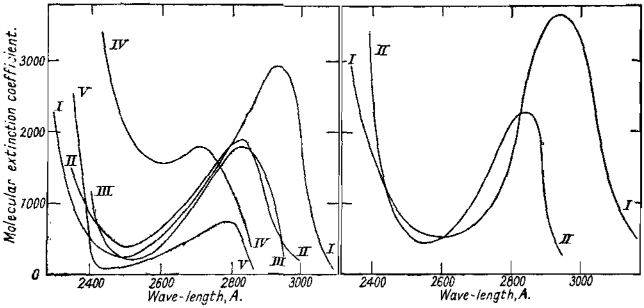
Since the appearance of Fernholz's publication we have synthesised several duroquino ethers in order to compare their properties with those of the tocopherols. Examinatior of the absorption spectra of these compounds revealed at once a remarkable differenc from the tocopherols. The collected data for the substances examined are shown ii Figs. 1 and 2.

Duroquinol and ψ-cumoquinol show single absorption maxima at about 2950 A. In thi connection it is worthy of mention that the spectrum given for duroquinol by Karre Salomon, and Fritzsche (*loc. cit.*) is incorrect. An absorption curve of the type the describe is only shown by partly oxidised solutions of duroquinol (observation of Dr. F Waldmann; cf. also John, *loc. cit.*). This oxidation occurs with extreme ease and a accurate spectrum can only be obtained if a freshly prepared duroquinol solution is examine The mono-ethers of duroquinol also show a maximum, but it occurs at about 2830 A. an is of smaller intensity (mono-acylation of duroquinol causes a similar shift of the maximum introduction of a second ether grouping as in the dicetyl ether causes a slight shift in t position of this maximum. Esterification of a mono-ether as in O-*benzoylduroquinol al ether* causes a further shift of the maximum to about 2710 A.

α-Tocopherol (John, *loc. cit.*) and β-tocopherol show a single absorption maximum at 2950 A. and allophanation of the hydroxyl group (cf. John, *loc. cit.*) causes a shift of the maximum to about 2860 A. accompanied by a marked fall in intensity. On this evidence alone the view that either α- or β-tocopherol is a simple duroquinol ether is highly improbable.

Further evidence pointing in the same direction was obtained by comparing the behaviour of the various compounds towards silver nitrate. Duroquinol, ψ-cumoquinol, and the tocopherols all reduce methyl-alcoholic silver nitrate on warming. This property is not shown by the duroquinol ethers we have prepared, although, of course, the mono-ethers will reduce ammoniacal silver nitrate. Finally, we were unable to isolate either duroquinol or ψ-cumoquinol from the products obtained on heating β-tocopheryl allophanate with hydriodic acid or with hydrochloric acid in acetic acid.

FIG. 1. FIG. 2.




I. *Duroquinol in ether.*
II. *Monocetylduroquinol in alcohol.*
III. *Monoallylduroquinol in alcohol.*
IV. *O-Benzoylallylduroquinol in ether.*
V. *Dicetylduroquinol in ether.*

I. *β-Tocopherol in alcohol.*
II. *β-Tocopheryl allophanate in alcohol.*

*Duroquinol monocetyl ether* undergoes pyrolysis much more rapidly than α- or β-tocopherol and at a slightly lower temperature (*ca.* 325°); the crude crystalline distillate of duroquinol has a m. p. above 220° and is already practically pure. The corresponding *dicetyl* ether decomposes at about the same rate as the tocopherols and again yields a very pure product. As mentioned above, we observed the production of both ψ-cumoquinol and duroquinol on pyrolysis of our active materials. We have re-investigated this, using for pyrolysis a specimen of β-tocopherol prepared from a five-times recrystallised sample of the allophanate. Here again we obtained ψ-cumoquinol as the main product, but by washing the crude crystalline distillate, m. p. 160—170°, with ether a small, less soluble fraction of quinol was obtained, m. p. 195—200° with considerable sublimation. The total yield of crystalline material being only about 3% of the weight of tocopherol used, it was impossible for us, with the quantities at our disposal, to identify this material properly. The possibility admittedly exists that our β-tocopheryl allophanate was contaminated with the α-compound, but we consider this highly unlikely. Pyrolysis of a very small amount of α-tocopherol yielded a crude crystalline material of m. p. between 180° and 190°, again suggestive of a mixture of duroquinol with a lower-melting quinol, when contrasted with the behaviour of duroquinol cetyl ether. The evidence is admittedly not conclusive, but we consider it at least possible that both α- and β-tocopherol yield mixtures of ψ-cumoquinol and duroquinol on pyrolysis.

As has been pointed out by Evans, Emerson, and Emerson (*loc. cit.*) α-tocopheryl

allophanate does not behave like an unsaturated compound towards bromine or potassium permanganate; the same is true of β-tocopheryl allophanate. Work on the oxidative degradation of β-tocopherol has been hampered by scarcity of material, but oxidation of the allophanate with alkaline potassium permanganate gave an acid yielding a *p-phenylphenacyl* ester, m. p. 84°. The small amount available precluded complete identification, but it appeared from analysis to be an aliphatic acid containing about 18 carbon atoms. Catalytic hydrogenation of β-tocopherol is difficult to effect, but 4 mols. of hydrogen were taken up slowly on heating. The allophanate also absorbed 4 mols. of hydrogen, but here, curiously enough, 1 mol. was rather easily taken up.

The properties of α- and β-tocopherol so far as they are known indicate that they are in some way related to duroquinol and ψ-cumoquinol. The absorption of 4 mols. of hydrogen by β-tocopherol, coupled with the apparently saturated nature of its allophanate, suggests the possibility that it may be a cyclic ether, *i.e.*, a coumaran or chroman derivative bearing a long side chain in the heterocyclic nucleus. A similar structure would be expected for α-tocopherol. Such a structure for these compounds might also explain the production of a mixture of quinols on pyrolysis. This possibility is at present being investigated by degradative and synthetic methods, and our results will be communicated later. As a preliminary model we have examined 5-hydroxy-4 : 6 : 7-trimethyl*iso*coumaranone (III) (Smith and MacMullen, *J. Amer. Chem. Soc.*, 1936, **58**, 630). This compound we find shows a striking resemblance to the tocopherols in both its absorption spectrum (max. *ca.* 2930 A., min. 2650 A.) and reducing properties.

As regards the molecular size of β-tocopheryl allophanate our analysis figures do not permit of a differentiation between $C_{30}H_{50}O_4N_2$ and $C_{31}H_{52}O_4N_2$. Miss D. M. Crowfoot, to whom we are greatly indebted, has made a crystallographic examination of β-tocopheryl allophanate. Her results, reproduced in the experimental section, are indicative of a $C_{30}$ formula for this compound, corresponding to a $C_{28}$ formula for β-tocopherol itself.

## Experimental.

*α-Tocopheryl Allophanate.*—The purified substance had m. p. 158—159° and its properties were in agreement with those given by Evans, Emerson, and Emerson (*loc. cit.*) (Found : C, 72·3; H, 10·0. Calc. for $C_{31}H_{52}O_4N_2$ : C, 72·0; H, 10·2%). In chloroform solution it was optically inactive. α-Tocopherol was obtained from it by hydrolysis as a colourless oil.

*β-Amyrin Allophanate from Crude β-Tocopheryl Allophanate.*—The crude β-tocopheryl allophanate, m. p. *ca.* 138° (cf. Part II, *loc. cit.*), shows a reddish-violet colour in the Liebermann reaction, whereas the pure allophanate, m. p. 143·5—144·5°, does not. Purification is best effected by boiling methyl-alcoholic solutions with charcoal; the charcoal, then eluted with acetone, yields small amounts of a beautifully crystalline allophanate, m. p. 273—275°, showing the reddish-violet Liebermann reaction characteristic of β-amyrin derivatives. Mixed with a specimen of β-amyrin allophanate (m. p. 272—273°), it produced no depression of the m. p.

*Micro-hydrogenations.*—β-Tocopherol (1·02 mg.), $C_{29}H_{50}O_2$, absorbed 0·2055 c.c. of hydrogen at N.T.P. (= 3·87 mols. $H_2$). The solvent was decalin–acetic acid, and the catalyst platinum oxide. No absorption occurred in the cold, but slow regular absorption occurred at 90° and was complete after 8 hours.

β-Tocopheryl allophanate (1·905 mg.), $C_{31}H_{52}O_4N_2$, absorbed 0·3274 c.c. of hydrogen at N.T.P. (= 3·96 mols. $H_2$), the solvent being acetic acid, and the catalyst platinum oxide. One mol. of hydrogen was absorbed in the cold, and the remainder by heating the mixture to 90°, shaking it until it was cold, and keeping it for 12 hours.

*Attempted Acid Fission of β-Tocopherol.*—β-Tocopheryl allophanate (100 mg.) was heated in a sealed tube at 200° with hydrochloric–acetic acid (5 c.c. of a mixture of 10 c.c. of glacial acetic acid and 30 c.c. of concentrated hydrochloric acid saturated with hydrogen chloride at 0°) during 18 hours. After a further 2 hours at 220° the tube was cooled, and the dark gummy product extracted with ether. The ethereal solution, on drying and evaporating, gave a dark brown gum which did not crystallise. Oxidation with ferric chloride gave a mixture which had a slight quinone-like odour, but no appreciable steam-volatile product could be detected. The combined material from this experiment was refluxed for 3 hours with hydriodic acid (*d* 1·7), and the product submitted to chromatographic analysis on aluminium oxide (Merck). A small amount of a yellowish oil was washed through the column. The rest of the material, which was

very strongly absorbed, was a brown gum; this did not crystallise, nor did it appear to give a volatile quinone on oxidation.

*Oxidation of β-Tocopheryl Allophanate.*—The allophanate (145 mg.), dissolved in pure hexane (50 c.c.), was shaken for 12 hours with a solution of potassium permanganate (570 mg. = 19 mols.) in sodium hydroxide solution (75 c.c. of 3%). Much of the permanganate was then unchanged and the concentration of alkali was increased to 6% and shaking continued for a further 24 hours. The hexane layer was separated and gave on evaporation a small amount of a substance, m. p. 140°, possibly unchanged allophanate. The aqueous layer was freed from manganese dioxide and unchanged permanganate by means of sulphur dioxide, and the resulting solution, after acidification with sulphuric acid, was extracted continuously with ether during 48 hours. The extract was shaken with alkali. A small amount of an unidentified neutral oil remained in the ether, and the acidic material was recovered by acidifying the alkaline layer and again extracting it with ether. Evaporation of this ethereal extract gave a thick oil (26 mg.). This oil had no detectable rotation in chloroform solution ($c = 0{\cdot}65\%$; $l = 1$ dm.) and titration against N/20-sodium hydroxide indicated a mol. wt. of about 260, assuming it to be a monobasic acid. The material was esterified with *p*-phenylphenacyl bromide, and the *ester* crystallised from methyl alcohol. After several recrystallisations a product, m. p. 84°, was obtained (Found: C, 80·7; H, 9·4. $C_{33}H_{46}O_3$ requires C, 80·3; H, 9·6%. $C_{33}H_{44}O_3$ requires C, 80·7; H, 9·3%). A portion of the crude acidic material remained unesterified in this experiment.

*Pyrolysis of Active Concentrates from Wheat Germ Oil.*—The oil (600 mg.), prepared by the method described in Part II (*loc. cit.*) and showing vitamin E activity in a dosage of 15 mg., was heated in a nitrogen atmosphere to about 360° in a bulb tube with a long side arm. From about 300° onwards a yellowish oil distilled, followed at 350—360° by a product which crystallised in colourless needles in the side tube. After about 20 minutes the distillation was complete. The crystalline distillate was freed from oily impurities by washing with a little light petroleum (b. p. 40—60°); it had a rather indefinite m. p. 170—180°. The material was recrystallised from petroleum (b. p. 100—120°) and the crystals (A) separating were washed with low-boiling petroleum, the washings being combined with the crystallisation mother-liquors (B).

The crystals (A) were treated with a little sodium hyposulphite solution, filtered off, and sublimed in a vacuum. The sublimate was again washed with light petroleum, then with a very small amount of ether, and again sublimed. The product (*ca.* 6 mg.), which had the crystalline form of duroquinol, had m. p. 223—224° (Found: C, 72·5; H, 8·6. Calc. for $C_{10}H_{14}O_2$: C, 72·3; H, 8·4%). A mixed m. p. with synthetic duroquinol showed no depression, and oxidation with ferric chloride gave a yellow quinone, m. p. 107—108°, undepressed by duroquinone (m. p. 108—109°).

The combined liquors and washings (B) were evaporated, and the residue washed with sodium hyposulphite solution and taken up in ether. The dried ethereal solution was evaporated, and the residue purified by crystallisation from light petroleum (b. p. 60—80°) and sublimation in a vacuum. The product (2·5 mg.) had m. p. 165—166° (Found: C, 70·7; H, 8·1. Calc. for $C_9H_{12}O_2$: C, 71·1; H, 7·9%). A mixed m. p. with ψ-cumoquinol (m. p. 168—170°) showed no depression and oxidation with ferric chloride gave a yellow quinone, m. p. 28—30° (ψ-cumoquinone has m. p. 30°).

The relative proportions of the two quinols varied in different experiments even with the same sample of oil.

*Duroquinol Cetyl Ethers.*—A mixture of duroquinol (3 g.), methyl ethyl ketone (80 c.c.), cetyl iodide (6·3 g.), and anhydrous potassium carbonate (2·55 g.) was refluxed in a nitrogen atmosphere during 10 hours. The mixture was now filtered, and the filtrate kept at 0° for a few hours. The crystalline material which separated was dissolved in light petroleum (b. p. 40—60°), and the filtered solution evaporated. The residue, recrystallised from acetone, gave *duroquinol dicetyl ether* in colourless waxy crystals, m. p. 81—84° to a cloudy liquid which became clear at 86—87° [Found: C, 82·0; H, 12·5; *M* (Rast), 550. $C_{42}H_{78}O_2$ requires C, 82·2; H, 12·5%; *M*, 614].

The methyl ethyl ketone filtrate from the dicetyl ether was evaporated to dryness, and the residue freed from remaining traces of the latter compound by dissolution in cold acetone. The acetone solution was now steam-distilled to remove duroquinone, and the distillation residue shaken with light petroleum. A yellow solid (0·85 g.) remained undissolved; it had m. p. 204—205° after recrystallisation from methyl alcohol and was probably diduroquinone (v. Pechmann, *Ber.*, 1889, **22**, 2115). The light petroleum solution was washed with aqueous caustic potash, then with water, dried over sodium sulphate, and evaporated. The residue was taken up in a small amount of acetone, in which *duroquinol monocetyl ether* is readily soluble, filtered, and cooled to − 5°. The crystalline material which separated had m. p. 91—92°, but

still contained traces of iodine (contamination with cetyl iodide). By repeated crystallisation from methyl alcohol and finally from light petroleum (b. p. 60—80°) the ether was obtained in colourless waxy crystals, m. p. 98° (Found: C, 79·4; H, 11·4. $C_{26}H_{46}O_2$ requires C, 80·0; H, 11·7%). On oxidation with chromic acid by the Kuhn–Roth method the substance gave 3·2 mols. of acetic acid. It showed no vitamin E activity when tested biologically in doses up to 50 mg.

At about 325° the monocetyl ether decomposes within a few minutes, giving duroquinol (m. p. crude 221°). The dicetyl ether behaves similarly, but the decomposition occupies about 20 minutes (m. p. of crude duroquinol 225—227°). The yield in each case is *ca.* 20% of the theoretical.

O-*Monobenzoylduroquinol.*—To a solution of duroquinol (5·2 g.) in dry pyridine (26 c.c.) at 0°, benzoyl chloride (3·8 c.c.) was added dropwise with shaking, the whole operation being carried out in an atmosphere of nitrogen. After standing overnight, the mixture was heated on the water-bath for 1 hour, cooled, and poured on a mixture of ice and dilute sulphuric acid. The solid which separated was collected, washed thoroughly first with sodium hydroxide solution, then with water, dried, and boiled with methyl alcohol (80 c.c.); this treatment left much of the product undissolved but removed duroquinone and unchanged duroquinol. After cooling, the suspension was filtered; the filter residue (5·2 g.) had m. p. 204—215°. The product was extracted three times with a mixture of benzene (4 parts) and petroleum (7 parts; b. p. 100—120°), which removed the more soluble dibenzoyl derivative. The residue (4 g.), m. p. 220—221°, gave after two recrystallisations from methyl alcohol colourless prismatic needles of O-*monobenzoylduroquinol*, m. p. 221—223° (Found: C, 75·6; H, 6·4. $C_{17}H_{18}O_3$ requires C, 75·6; H, 6·6%).

O-*Benzoylduroquinol Allyl Ether.*—*O*-Monobenzoylduroquinol (0·6 g.) was added to potassium powder (0·1 g.) in toluene (20 c.c.) and heated, a thick gelatinous mass being formed. When most of the potassium had disappeared, allyl bromide (0·24 c.c.) was added together with more dry toluene (10 c.c.), and the whole refluxed for *ca.* 4 hours; the gelatinous material then disappeared and potassium bromide separated. The liquid was now filtered and evaporated to dryness, yielding a thick oil which crystallised on trituration with light petroleum. Recrystallised from methyl alcohol, O-*benzoylduroquinol allyl ether* formed colourless needles (0·4 g.), m. p 111—112° (Found: C, 76·9; H, 7·0. $C_{20}H_{22}O_3$ requires C, 77·4; H, 7·1%).

*Duroquinol Monoallyl Ether.*—The above benzoate was refluxed in a nitrogen atmospher with methyl-alcoholic potassium hydroxide (5%) during 2 hours. The resulting solution wa diluted with water and extracted with ether, and the extract dried and evaporated. The oily residue crystallised from light petroleum (b. p. 40—60°) in colourless needles, m. p. 108° (Found C, 75·8; H, 8·8. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%). The substance reduced ammoniaca methyl-alcoholic silver nitrate solution but had no action on methyl-alcoholic silver nitrate alone even on heating. Duroquinol monocetyl ether also may be prepared in an analogous manne *via* the benzoyl derivative; a sample thus prepared had m. p. 102°.

*Migration Experiments.*—When a solution of *O*-benzoylduroquinol allyl ether in dimethy aniline was refluxed for 6 hours, the allyl group was removed and *O*-monobenzoylduroquino m. p. 221—223°, was isolated in nearly quantitative yield. On similar treatment duroquin monoallyl ether yielded duroquinone (oxidation of initially formed quinol), but duroquin monocetyl ether was recovered unchanged.

*Crystallographic Data.*—β-Tocopheryl allophanate crystallises in the monoclinic space grou $P_2$; $a$ = 13·52 A. (limits, 13·57, 13·45); $b$ = 5·26 A. (limits 5·27, 5·245); $c \sin \beta$ = 21·35 (limi 21·40, 21·05); $\rho$ = 1·092 (limits 1·097, 1·087). The number of molecules in the unit cell bei taken as 2, the minimum molecular weight required by the crystallography is 502 (limits 5( 490). This indicates definitely a $C_{30}$ formula ($C_{30}H_{50}O_4N_2$ requires *M*, 502).

We are indebted to Mr. F. Boston, Manchester University, for the micro-hydrogenati figures. Our thanks are also due to Messrs. Glaxo Laboratories Ltd. and Messrs. Hoffma La Roche & Co. for their generous assistance and gifts of material and to Dr. E. L. Smith of t former firm for measuring many absorption spectra. We have to thank Miss. A. M. Coppi who has undertaken the biological testing necessary in these investigations, and the Medi Research Council, whose grant to her has made this possible.

(Note added, February 11th) Emerson, Emerson, Mohammad, and Evans (*J. Biol. Che* 1937, **122**, 99) have now reported that their purified β-tocopheryl allophanate has m. p. 144—14

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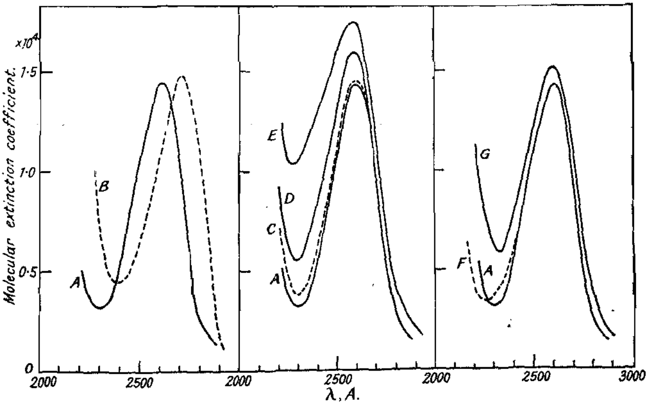
## 50. *Constitution of the Purine Nucleosides. Part VI. Adenine Deoxyriboside, Adenine Glucoside, and a Route to the Synthesis of the Naturally Occurring Nucleosides.*

By J. Masson Gulland and Leonard F. Story.

Comparisons of the ultra-violet absorption spectra of adenine deoxyriboside from thymus nucleic acid and of synthetic adenine glucoside with the spectra of 7- and 9-methyladenines show that both these nucleosides are 9-substituted adenines. This means that the purine nucleosides and nucleotides of thymus nucleic acid are similar in constitution to the corresponding derivatives of yeast nucleic acid. It is also important in being the first occasion on which a synthetic purine nucleoside has been recognised as having the carbohydrate radical in the same position as have the natural nucleosides. As a result, a route is open to the synthesis of the naturally occurring nucleosides, and enzyme experiments should shed light on the question of the presence of an α- or a β-glycosidic linkage in these compounds.

In Parts IV and V (J., 1934, 1639; 1937, 1912) the carbohydrate radicals of adenosine and adenine thiomethylpentoside were assigned to the 9-position of the adenine molecule by reason of the close resemblance of their ultra-violet absorption spectra to those of 9-methyladenine, and the dissimilarity of the spectra of 7-methyladenine (Fig. 1, taken from Part IV).

Fig. 1. Fig. 2. Fig. 3.




A. *9-Methyladenine in water*, N/20-HCl *and* N/20-NaOH.

Fig. 1.

B. *7-Methyladenine in water and* N/20-HCl.

Fig. 2.

C. *Adenine deoxyriboside* (M/80,000) *in water.*
D. *Adenine deoxyriboside* (M/75,000) *in* N/20-HCl.
E. *Adenine deoxyriboside* (M/100,000) *in* N/20-NaOH.

Fig. 3.

F. *Adenine* d-*glucoside* (M/80,000) *in water and* N/20-HCl.
G. *Adenine* d-*glucoside* (M/80,000) *in* N/20-NaOH.

The method has now been applied to the determination of the positions of the carbohydrate radicals in adenine deoxyriboside (Klein, *Z. physiol. Chem.*, 1934, **224**, 244)

and adenine *d*-glucoside (Fischer and Helferich, *Ber.*, 1914, **47**, 210). Both these are now shown to be 9-substituted adenines.

The interest of these results lies in the following facts. First, the purine nucleosides derived from thymus nucleic acid, and the corresponding nucleotides, are constituted similarly to the nucleosides and nucleotides of yeast nucleic acid as regards the position of the sugar radicals.

Secondly, this is the first occasion on which a synthetic purine nucleoside has been shown to have the carbohydrate radical in the same position as have the natural nucleosides. Theophylline *d*-glucoside and *l*-arabinoside, prepared from silver theophylline and the appropriate acetylated bromo-sugar, are 7-substituted derivatives of theophylline (Gulland, Holiday, and Macrae, J., 1934, 1639), and the same conclusion presumably applies to theophylline rhamnoside (Fischer and Fodor, *Ber.*, 1914, **47**, 1058), *d*-galactoside (Helferich and Kühlewein, *Ber.*, 1920, **53**, 17), *iso*rhamnoside (Fischer, Helferich, and Ostmann, *ibid.*, p. 873), *d*-xyloside and *d*-riboside (Levene and Sobotka, *J. Biol. Chem.*, 1925, **65**, 463), all of which are obtained from theophylline silver.

Thirdly, it follows that dichloroadenine *d*-glucoside and chloroadenine *d*-glucoside (both obtained as intermediates in the preparation of adenine glucoside), hypoxanthine *d*-glucoside (formed from adenine glucoside by the action of nitrous acid), and guanine *d*-glucoside (prepared from chloroadenine glucoside) are all also 9-substituted derivatives. These results provide a route to the synthesis of the naturally occurring purine nucleosides, the appropriate carbohydrate derivatives being used. Moreover, a study of the action of nucleosidases on such synthetic nuclebsides should throw light on the question of the presence of an α- or a β-glycosidic linkage in the naturally occurring nucleosides. Experiments along these lines are in progress.

## EXPERIMENTAL.

Adenine deoxyriboside, for a pure specimen of which we are much indebted to Dr. W. Klein, was prepared by the fission and dephosphorylation of thymus nucleic acid by a preparation of mixed thymonucleinase and phosphomonoesterase from calf's intestinal mucosa (Klein, *Z. physiol. Chem.*, 1933, **218**, 164) in presence of silver ions, which inhibit the action of the accompanying deaminase. Its ultra-violet absorption spectrum in aqueous solution resembles that of 9-methyladenine, and in acid and in alkaline solutions a slight increase in the value of the extinction coefficient occurs without change of the wave-length (2600 A.) of the peak (Fig. 2), a behaviour similar to that observed in the case of adenine thiomethylpentoside in alkaline solution. It is doubtful whether the measurement of the spectrum in acid solution is valid owing to the ease with which this reagent hydrolyses the glycosidic linkage of adenine deoxyriboside.

For the preparation of adenine glucoside, potassium urate was converted into 2 : 8 dichloroadenine through the stages of 2 : 6-dichloro-8-hydroxypurine and 2 : 6 : 8-trichloropurine (Fischer and Ach, *Ber.*, 1897, **30**, 2208). In the formation of trichloropurine by heatin[g] dichlorohydroxypurine with phosphorus oxychloride a silver-lined steel bomb was found to b[e] more convenient than sealed glass tubes, and the use of a mixture of phosphorus trichlorid[e] (1 part) and oxychloride (3 parts) instead of pure oxychloride gave better, but fluctuating yields, although these were never as high as those recorded by Fischer and Ach.

Since the interaction of the sodium salt of dichloroadenine with methyl iodide yiel[ds] dichloro-9-methyladenine (Fischer, *Ber.*, 1897, **30**, 2238), it seemed possible that the interactio[n] of the silver salt with tetra-acetobromoglucose would also give rise to a 9-substitute[d] compound. The silver salt of dichloroadenine, prepared by the addition of ammoniacal silv[er] nitrate solution to an ammoniacal solution of dichloroadenine, was collected, washed wi[th] water, and dried by distillation of its suspension in toluene (Gulland and Macrae, J., 193[3,] 662). The subsequent condensation with tetra-acetobromoglucose, the deacetylation of t[he] product with methyl-alcoholic ammonia, and the replacement of the chlorine atoms [by] hydrogen through reduction with hydriodic acid and phosphonium iodide followed t[he] procedures of Fischer and Helferich (*Ber.*, 1914, **47**, 227), the adenine glucoside being fina[lly] purified through the picrate. When heated in a melting-point apparatus, the glucos[ide] showed the characteristic behaviour described by Fischer and Helferich.

The ultra-violet absorption spectra of adenine glucoside in aqueous and in acid soluti[on]

(peak at 2600 A.) were identical with those of 9-methyladenine; the spectrum in alkaline solution showed a slight increase in the value of the extinction coefficient (Fig. 3).

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UNIVERSITY COLLEGE, NOTTINGHAM. [*Received, January 4th*, 1938.]

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## 51. *An Extension of the Macleod Equation.*

By DAVID T. LEWIS.

It is suggested that the Macleod constant is a function of the critical temperature of a substance, and it has been established that for similar groups of substances, the critical temperatures, boiling points, and molar heats of vaporisation are connected with the parachor values by simple linear relationships. Divergence from these relationships is taken as evidence of association.

By utilising these generalisations, values for the various physical constants of certain elements have been calculated; parachor values so obtained exhibit close agreement with those suggested by Sugden from a study of the periodic variation of the parachor.

MACLEOD (*Trans. Faraday Soc.*, 1923, **19**, 38) has shown that the surface tension $\gamma$ may be connected with the density of the liquid and of the vapour at the same temperature, $D$ and $d$ respectively, by means of the equation

$$\gamma = C(D - d)^4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The constant $C$ is unaffected by increase of temperature for normal liquids, but shows a slight and steady rise for associated liquids.

Fowler (*Proc. Roy. Soc.*, 1937, *A*, **153**, 229) has derived this equation in the form

$$\gamma = \frac{B}{4A^2T_c}\left(\frac{n}{V} - \frac{n'}{V}\right)^4 = \frac{B}{4mA^2T_c}(D - d)^4 \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $n/V$, $n'/V$ represent the average molecular densities, $m$ is the mass of the molecule, $A = 12n^2/V_c^2T_c$ is a constant for one particular substance, and $B$ is an integral function whose evaluation for an individual element requires a precise knowledge of atomic dimensions, and of the interaction energy $E_r$ for a pair of molecules. This equation has been shown to yield satisfactory values for the parachor values of argon and mercury, but its general application to a complete chemical group is rendered difficult owing to lack of precise data for the evaluation of $B$ and $A$. It does indicate, however, that there may exist a simple connection between the parachor values, $P$, and the critical temperatures, $T_c$, of various elements.

Katayama (*Sci. Rep. Tôhoku Imp. Univ.*, 1916, **4**, 373) has suggested an equation of the form

$$\gamma[M/(D - d)]^{2/3} = k(T_c - T) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Elimination of $\gamma$ between (1) and (3) gives for the Macleod constant

$$C = k(T_c - T)/M^{2/3}(D - d)^{10/3} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Mathias ("Le Point Critique des Corps Purs," 1904, p. 164) has shown that, in accordance with the law of rectilinear diameter, the critical density $D_c$ may be calculated by means of the equation

$$D_c = M/V_c = (D - d)/2(2 - T/T_c) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

It is not generally realised that this equation was suggested in a modified form by Thorpe

and Rucker (J., 1884, **45**, 135), who demonstrated the exact nature of its application. Substituting for $(D - d)$ in equation (4), we have

$$C = k(T_c - T)/M^4[(4T_c - 2T)/V_cT_c]^{10/3} \quad . \quad . \quad . \quad . \quad . \quad (6)$$

This formula also indicates that the Macleod constant should be dependent on the critical temperature. Curiously enough, the above function does not vary appreciably when the values concerned are fairly remote from the critical point. In the following table $k$ has been given the value 2·3, although it is well known that it varies slightly from substance. The experimental data are taken from Sugden (" The Parachor and Valency," 1930, p. 27).

*Benzene.*

($T_c$ = 288·5°; $V_c$ = 256·5 c.c.)

| | | | | | | |
|---|---|---|---|---|---|---|
| $t$ | 20° | 61° | 90° | 180° | 210° | 280° |
| $C^{1/4}$ (calc.) | 2·634 | 2·634 | 2·630 | 2·52 | 2·190 | 1·520 |
| $C^{1/4}$ (obs.) | 2·638 | 2·647 | 2·646 | 2·641 | 2·657 | 3·372 |

The value for $C$ given by equation (6) must be erroneous, for it predicts that the Macleod constant should become zero at the critical temperature whereas experimental results show that it tends to retain its normal value. Both this equation and Fowler's (*loc. cit.*) indicate that $C$ should be a function of the critical temperature, and from a survey of the available data it is suggested that the Macleod equation be rewritten in the form

$$\gamma = [(T_c - \alpha)/MK]^4(D - d)^4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

in which $M$, the molecular weight, occurs to the fourth power as in (6). The constants $\alpha$ and $K$ remain the same for one distinct chemical group and are probably configurational or cohesional functions characterising a particular type of molecule. Their values are determined from known data.

Sugden (*op. cit.*, p. 30) has defined the parachor as being given by $MC^{1/4}$, whence it follows that

$$P = (T_c - \alpha)/K \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

*i. e.*, the parachor for similar substances should be a linear function of the critical temperatures. This has been found to be the case for all the groups so far examined. The following equations have been derived from a graphical study of such groups.

| Group. | Equation. | Group. | Equation. |
|---|---|---|---|
| Inert gases | $T_c = 3{\cdot}7P - 48$ | Methyl fluoride group | $T_c = 3{\cdot}43P + 39$ |
| Halogens, including BrCl, etc. | $T_c = 5{\cdot}57P - 188$ | Ethyl fluoride group | $T_c = 3{\cdot}21P - 20$ |
| Halogen acids | $T_c = 2{\cdot}72P + 130$ | Fluorobenzene group | $T_c = 2{\cdot}33P + 63$ |

For a large number of substances it has been pointed out by Sugden (*op. cit.*) that the function $P/V_c$ is approximately constant and has the value 0·77. This rule does not apply with the inert gases. In the following table it will be seen that, although the parachors decrease linearly with the critical temperatures, there is no precise connection between them and the critical volume; moreover, the critical volume of helium is greater than that of neon although the parachor value is less.

| Substance. | $P$. | $T_c$, K. | $V_c$. | $T_b$, K.* | $T_c/T_b$. | $P/V_c$. |
|---|---|---|---|---|---|---|
| Helium | 20·5 | 33·0° | 57·7 | 4·1° | 8·048 | 0·3553 |
| Neon | 25·0 | 44·3 | 41·7 | 27·1 | 1·634 | 0·5995 |
| Argon | 54·0 | 151 | 75·3 | 87·3 | 1·730 | 0·7171 |
| Krypton | 68·0 | 210 | 92·0 | 121·2 | 1·733 | 0·7391 |
| Xenon | 91·0 | 289·6 | 112·7 | 163·9 | 1·767 | 0·8076 |

* $T_b$ is the boiling point.

The previous equations being accepted, the parachors of various substances can calculated from their known critical temperatures. The following table shows the applability of these relationships, $P$ (S) being the values calculated from Sugden's atomic constants.

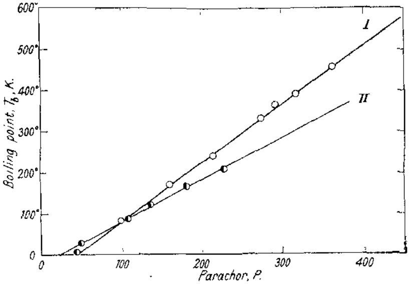
| Substance. | $T_c$, K.* | P (calc.). | P (S). |
|---|---|---|---|
| He | 33·0° | 21·9 | 20·5 † |
| Ne | 44·3 | 25·0 | 25·0 † |
| A | 151·0 | 53·78 | 54·0 † |
| Cl | 416·9 | 108·6 | 108·6 |
| Br | 575·4 | 137·0 | 136·0 |
| HF | 246·4 ‡ | — | 42·8 |
| HCl | 324·1 | 71·36 | 71·4 |
| $C_6H_5F$ | 559·0 | 212·9 | 215·7 |
| $C_6H_5Cl$ | 632·0 | 244·2 | 244·3 |
| Kr | 210·0° | 69·72 | (68) |
| Xe | 289·6 | 91·22 | (91) |
| Rn | 377·0 | 114·9 | — |
| I | 826·0 | 182·0 | 182·0 |
| F | 99·4 ‡ | — | 51·4 |
| HBr | 363·0 | 85·67 | 85·1 |
| HI | 424·0 | 108·1 | 108·1 |
| $C_6H_5Br$ | 670·0 | 260·5 | 258·0 |
| $C_6H_5I$ | 721 | 281·8 | 281·0 |

* Critical constants are taken from Lange's "Handbook of Chemistry and Physics," p. 897; Pickering, *J. Physical Chem.*, 1924, **28**, 97; and "International Critical Tables," Vol. III, p. 230.

† Experimental data (Sugden, *op. cit.*).

‡ Calculated from known parachor.

In the above table, the critical temperatures of fluorine and undissociated hydrogen fluoride, being unknown, have been calculated from the known parachor values. In the other cases the parachor values have been computed from existing data; those given for the first three inert gases are values determined at the Leiden laboratories. The values for krypton and xenon were suggested by Sugden from a study of the periodic variation of the parachor and agree very well with the calculated values. A probable value for radon appears to be 114·9




Where there is association, *e.g.*, as with hydrogen fluoride, there is a distinct departure from the linear relationship obeyed by the other members of the family. It is not possible, through lack of data, to apply these equations to many substances, but it has been observed that the plot of the boiling points, $T_b$, against the parachor values gives a relation which is as precise as when the critical temperatures are used. The graphs, I and II respectively, give the plot of the boiling points of the halogens (including halogen halides) and the inert gases against their respective parachor values as abscissæ.

This agreement suggests that there should be a very precise connection between the boiling points and the critical temperatures of chemically related elements, and this has been investigated by Pawlewski (*Ber.*, 1882, **15**, 460) and Guldberg (*Z. physikal. Chem.*, 1890, **5**, 374). The latter demonstrated that for closely related substances, the ratio $T_c/T_b$ was very nearly constant. If we consider the two derived equations for the inert gases, *viz.*, $T_c = 3{\cdot}7P - 48$ and $T_b = 2{\cdot}07P - 24{\cdot}6$, and eliminate $P$ it is apparent that a more accurate form of the Guldberg ratio would be $(T_c + \theta)/(T_b + \lambda)$, where $\theta$ and $\lambda$ are constants. The two ratios are compared in the following table.

| Substance. | $T_c$, K. | $T_b$, K. | $T_c/T_b$. | $(T_c + 48)/(T_b + 24{\cdot}6)$. |
|---|---|---|---|---|
| He | 33·0° | 4·1° | 8·048 | 2·832 |
| Ne | 44·3 | 27·1 | 1·634 | 1·785 |
| A | 151 | 87·3 | 1·730 | 1·778 |
| Kr | 210 | 121·2 | 1·733 | 1·775 |
| Xe | 289·6 | 163·9 | 1·767 | 1·791 |

The expected value for the constant is the quotient of the coefficients of $P$, *i.e.*, 1·786, and except with helium the fluctuation from this value is less than 1%.

By utilising the boiling point relation, an analysis has been made of the parachors of the alkali metals, whose boiling points fall regularly with increasing molecular volume. With Sugden's values for the parachors of sodium, potassium, and rubidium (*op. cit.*, p. 179), it will be found that a perfectly linear relationship is obtained with the boiling points, and if that of cæsium is accepted as 670°, a parachor value of 140 could be predicted for this substance. Sugden gives six values for this function derived from data concerning six different salts, and five of them are in the neighbourhood of this value. The sixth value, 153, is derived from the cæsium iodide, and in all cases iodides lead to higher values than other salts. It is suggested that $P = 140$ is the more correct value for cæsium, Sugden's provisional value being $150 \pm 10$. From the relatioships now described, many others can be derived. For example, it is obvious by Trouton's law that a perfectly linear relation will exist between the parachor and the molar heat of vaporisation. This has been verified by the author, and an application of this relation to the data of Durrant, Pearson, and Robinson (J., 1934, 731) corroborates their conclusion that in the phosphine family arsine and stibine are normal liquids, whereas phosphine, and to a much greater extent ammonia, are associated.

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## 52. *Acid Salts of Monobasic Organic Acids. Part IV. The Salting-out Effect.*

By John D. M. Ross, Thomas J. Morrison, and Cecil Johnstone.

The manner in which the extent of compound formation between mandelic acid and metallic mandelates is modified by the salting-out effects of the latter has been studied by an examination of the solubilities of the acid in a series of metallic chlorides and nitrates. After applying a correction for the salting-out effect of the metallic ions, we conclude that the extent of compound formation in all the systems studied is the same, and, therefore, independent of the nature of the metallic ion present. The extent of compound formation for racemic mandelic acid is found to be about twice as great as with the active acid.

The extent of compound formation between mandelic acid, both racemic and active, ar various metallic mandelates has already been studied by us (J., 1933, 1016; 1936, 86' 1937, 608). In all the systems examined it is notable that the solubility of racemic ar active mandelic acid increases with increasing concentration of the normal salt, where the law of mass action would lead one to expect a decrease in solubility on addition of a sa containing an ion in common with the acid. Larsson (*Z. physikal. Chem.*, 1930, **148**, 14 1931, **153**, 306) and Kolthoff and Bosch (*J. Physical Chem.*, 1932, **36**, 1685) have sho that the solubility of benzoic acid is increased by the addition of sodium and potassi benzoates, and a similar result is recorded by Osol and Kilpatrick (*J. Amer. Chem. Sc* 1933, **55**, 4430) for *o*-chlorobenzoic acid and its sodium salt.

Some of those investigators agree that the simplest way of explaining this increase solubility is to assume that complex formation of some type occurs in solution betw the acid and its salt, so that the active mass of the acid in solution is kept constant by dissolution of more acid. Since complexes can be isolated in the solid form from s solutions, this assumption seems to be justified.

The salts of *r*-mandelic acid affect its solubility to a decreasing extent in the follow order: Univalent ions, Cs > Tl > Rb > K > $NH_4$ > Na > Li; bivalent ions, Ba Sr > Mg. For the active acid and its salts the order of the effect is similar: Unival ions, Tl > Cs > Rb > K > $NH_4$ > Na > Li; bivalent ions, Sr > Ba > Ca > We might conclude from these results alone that the tendency towards acid salt forma is in both cases greatest for thallium and cæsium, and least for lithium and magnesi However, it is well known that metallic ions produce a salting-out effect, which is depen on the size of the ions, being greatest for the small lithium ions and least for the la

cæsium ions. This affects the solubility of the acid in the opposite direction to that of compound formation, which corresponds to a salting-in effect. By a study of the variation of the solubility of mandelic acid in presence of a series of chlorides and nitrates of the alkali and alkaline-earth metals, we have obtained data which enable us to calculate the extent of this salting-out effect, and so apply a correction for it.

It is found that the salting-out effects of the metallic ions on *r*-mandelic acid increase in the following order: $Cs < Rb < K < NH_4 < Na < Li$; $Ba < Sr < Mg$; and for the active acid the order is the same for the alkali metals, but $Sr < Ba < Ca < Mg$ for the alkaline earths. In Table I the solubility (g.-equiv./1000 g. of water) of mandelic acid is recorded along with the concentration of added salt ($c$) and the solubility ratio $s/s_0$, where $s$ and $s_0$ are the solubilities of mandelic acid in the salt solution and in water respectively. From these figures the values of $K$ have been found, $K$ being the well-known salting-out constant obtained from the equation $\log s/s_0 = Kc$ (Setschenow, *Mém. Acad. Imp. Sci. St. Petersburg*, **7**, 22, No. 6; *Z. physikal. Chem.*, 1889, **4**, 117). Since this equation holds accurately only for sparingly soluble weak electrolytes, $K$ cannot in this case be expected to be absolutely constant, and its average value from $c = ca.$ 0·1 to $c = ca.$ 0·4 has been chosen as representative: for values of $c$ less than 0·1, the value of $s/s_0$ differs very little from 1·0, and so calculated values of $K$ are unreliable.

TABLE I.

Solubility of *r*-mandelic acid = 1·335.
Solubility of (−)mandelic acid = 0·738.

| Acid, concn. | $s/s_0$. | $c$. | $K$. |
|---|---|---|---|
| *Cæsium r-mandelate.* | | | |
| 1·714 | 1·283 | 0·128 | 0·85 |
| 2·039 | 1·527 | 0·217 | 0·85 |
| | | Average = | 0·85 |
| *Cæsium (−)mandelate.* | | | |
| 0·777 | 1·054 | 0·112 | 0·20 |
| 0·857 | 1·161 | 0·210 | 0·30 |
| 0·971 | 1·316 | 0·310 | 0·38 |
| | | Average = | 0·30 |
| *Potassium r-mandelate.* | | | |
| 1·646 | 1·233 | 0·160 | 0·57 |
| 1·909 | 1·430 | 0·269 | 0·58 |
| 2·360 | 1·768 | 0·415 | 0·60 |
| | | Average = | 0·58 |
| *Potassium (−)mandelate.* | | | |
| 0·803 | 1·089 | 0·193 | 0·19 |
| 0·970 | 1·315 | 0·384 | 0·36 |
| | | Average = | 0·27 |
| *Lithium r-mandelate.* | | | |
| 1·413 | 1·058 | 0·100 | 0·25 |
| 1·491 | 1·117 | 0·200 | 0·24 |
| 1·555 | 1·165 | 0·250 | 0·26 |
| | | Average = | 0·25 |
| *Lithium (−)mandelate.* | | | |
| 0·756 | 1·024 | 0·146 | 0·08 |
| 0·766 | 1·039 | 0·186 | 0·09 |
| 0·788 | 1·068 | 0·246 | 0·11 |
| | | Average = | 0·09 |
| *Calcium r-mandelate.* | | | |
| (See p. 267.) | | | |
| *Calcium (−)mandelate.* | | | |
| 0·747 | 1·012 | 0·030 | 0·17 |
| 0·755 | 1·023 | 0·063 | 0·15 |
| 0·776 | 1·052 | 0·075 | 0·29 |
| | | Average = | 0·20 |

| Acid concn. | $s/s_0$. | $c$. | $K$. |
|---|---|---|---|
| *Thallous r-mandelate.* | | | |
| 1·583 | 1·186 | 0·112 | 0·66 |
| 1·790 | 1·341 | 0·177 | 0·71 |
| | | Average = | 0·68 |
| *Thallous (−)mandelate.* | | | |
| 0·874 | 1·184 | 0·153 | 0·48 |
| 0·915 | 1·240 | 0·222 | 0·42 |
| 1·084 | 1·470 | 0·324 | 0·51 |
| | | Average = | 0·47 |
| *Ammonium r-mandelate.* | | | |
| 1·598 | 1·197 | 0·171 | 0·46 |
| 2·050 | 1·536 | 0·366 | 0·51 |
| 2·330 | 1·746 | 0·476 | 0·51 |
| | | Average = | 0·49 |
| *Ammonium (−)mandelate.* | | | |
| 0·757 | 1·025 | 0·157 | — |
| 0·884 | 1·199 | 0·358 | 0·22 |
| 1·068 | 1·447 | 0·581 | 0·28 |
| | | Average = | 0·25 |
| *Barium r-mandelate.* | | | |
| 1·450 | 1·086 | 0·062 | 0·58 |
| *Barium (−)mandelate.* | | | |
| 0·783 | 1·060 | 0·129 | 0·21 |
| 0·815 | 1·105 | 0·166 | 0·26 |
| 0·840 | 1·139 | 0·198 | 0·28 |
| | | Average = | 0·25 |
| *Magnesium r-mandelate.* | | | |
| 1·407 | 1·054 | 0·130 | 0·18 |
| *Magnesium (−)mandelate.* | | | |
| 0·758 | 1·028 | 0·186 | 0·06 |
| 0·792 | 1·074 | 0·294 | 0·10 |
| | | Average = | 0·08 |

| Acid concn. | $s/s_0$. | $c$. | $K$. |
|---|---|---|---|
| *Rubidium r-mandelate.* | | | |
| 1·652 | 1·237 | 0·143 | 0·65 |
| 1·851 | 1·387 | 0·210 | 0·67 |
| | | Average = | 0·66 |
| *Rubidium (−)mandelate.* | | | |
| 0·766 | 1·039 | 0·100 | 0·17 |
| 0·837 | 1·135 | 0·200 | 0·27 |
| 0·922 | 1·250 | 0·300 | 0·32 |
| 1·035 | 1·403 | 0·400 | 0·37 |
| | | Average = | 0·28 |
| *Sodium r-mandelate.* | | | |
| 1·442 | 1·080 | 0·113 | 0·30 |
| 1·584 | 1·187 | 0·213 | 0·35 |
| 1·690 | 1·266 | 0·277 | 0·37 |
| | | Average = | 0·34 |
| *Sodium (−)mandelate.* | | | |
| 0·737 | 0·998 | 0·059 | — |
| 0·755 | 1·023 | 0·112 | — |
| 0·853 | 1·157 | 0·292 | 0·22 |
| 0·877 | 1·188 | 0·341 | 0·22 |
| 1·008 | 1·367 | 0·616 | 0·22 |
| | | Average = | 0·22 |
| *Strontium r-mandelate.* | | | |
| 1·380 | 1·031 | 0·031 | 0·43 |
| *Strontium (−)mandelate.* | | | |
| 0·776 | 1·052 | 0·104 | 0·22 |
| 0·812 | 1·101 | 0·140 | 0·30 |
| | | Average = | 0·26 |

The solubility of the acid was found in solutions of metallic chlorides and nitrates at concentrations up to 1·0 g.-equiv./1000 g. of water. In order to eliminate the effect caused

by the two electrolytes having no common ion, solubility determinations were carried out in solutions containing also the normal mandelate of the metal at a concentration of 0·05 g.-mol./1000 g. of water. This has the effect of reducing the degree of dissociation of the acid to a very small constant value, and eliminates the initial rise in solubility which would otherwise result from double decomposition of the components.

The chlorides, nitrates, and mandelic acid used were all purified as far as possible. Two identical experiments in which potassium chloride was used with (−)- and with (+)-mandelic acid having given the same results, the latter acid was employed in the experiments.

5 G. of a solution containing 0·05 mol. of mandelate per 1000 g. of water were taken for each solubility determination, and weighed portions of the chloride or nitrate added. Duplicate experiments were carried out in each case: in one, excess acid was stirred for 4—5 hours at 25°, and in the other, excess acid was dissolved at a higher temperature, allowed to crystallise at 25°, and stirred for the same time. The acid in the filtered solution was estimated by titration. Owing to their deliquescent nature, the concentration of the chlorides of lithium, calcium, and magnesium was found by titration.

In order to obtain comparative figures for thallous salts, experiments were carried out with the nitrate, the chloride being too sparingly soluble. The introduction of a nitrate ion in this case introduced a further complication, so it was deemed advisable to compare the effect with those of the nitrates of the alkali metals.

The experimental results are in Table II, the rows labelled *r* and (+) referring to *r*- and (+) mandelic acid respectively. Negative values of *K* represent a salting-out effect.

TABLE II.

*Cæsium chloride.*

| | Acid concn. | $s/s_0$. | *c*. | *K*. |
|---|---|---|---|---|
| *r* | 1·402 | 1·000 | 0·000 | — |
| *r* | 1·416 | 1·010 | 0·202 | +0·02 |
| *r* | 1·425 | 1·016 | 0·303 | +0·02 |
| *r* | 1·433 | 1·022 | 0·404 | +0·02 |
| | | | Average = | +0·02 |
| (+) | 0·744 | 1·000 | 0·000 | — |
| (+) | 0·747 | 1·004 | 0·101 | +0·02 |
| (+) | 0·751 | 1·009 | 0·202 | +0·02 |
| (+) | 0·758 | 1·016 | 0·404 | +0·02 |
| | | | Average = | +0·02 |

*Ammonium chloride.*

| | Acid concn. | $s/s_0$. | *c*. | *K*. |
|---|---|---|---|---|
| *r* | 1·356 | 1·000 | 0·000 | — |
| *r* | 1·295 | 0·955 | 0·101 | −0·20 |
| *r* | 1·232 | 0·909 | 0·202 | −0·21 |
| *r* | 1·171 | 0·864 | 0·353 | −0·18 |
| | | | Average = | −0·20 |
| (+) | 0·721 | 1·000 | 0·000 | — |
| (+) | 0·709 | 0·984 | 0·101 | −0·07 |
| (+) | 0·689 | 0·956 | 0·202 | −0·10 |
| (+) | 0·677 | 0·939 | 0·303 | −0·09 |
| (+) | 0·662 | 0·918 | 0·404 | −0·09 |
| | | | Average = | −0·09 |

*Barium chloride.*

| | Acid concn. | $s/s_0$. | *c*. | *K*. |
|---|---|---|---|---|
| *r* | 1·345 | 1·000 | 0·000 | — |
| *r* | 1·315 | 0·978 | 0·101 | −0·10 |
| *r* | 1·260 | 0·937 | 0·202 | −0·14 |
| *r* | 1·183 | 0·880 | 0·303 | −0·18 |
| | | | Average = | −0·14 |
| (+) | 0·733 | 1·000 | 0·000 | — |
| (+) | 0·716 | 0·977 | 0·085 | −0·12 |
| (+) | 0·680 | 0·927 | 0·171 | −0·20 |
| (+) | 0·663 | 0·905 | 0·341 | −0·13 |
| | | | Average = | −0·15 |

*Rubidium chloride.*

| Acid concn. | $s/s_0$. | *c*. | *K*. |
|---|---|---|---|
| 1·332 | 1·000 | 0·000 | — |
| 1·252 | 0·940 | 0·202 | −0·13 |
| 1·167 | 0·876 | 0·505 | −0·12 |
| | | Average = | −0·13 |
| 0·738 | 1·000 | 0·000 | — |
| 0·729 | 0·988 | 0·101 | −0·05 |
| 0·717 | 0·971 | 0·202 | −0·06 |
| 0·697 | 0·945 | 0·404 | −0·06 |
| | | Average = | −0·06 |

*Sodium chloride.*

| Acid concn. | $s/s_0$. | *c*. | *K*. |
|---|---|---|---|
| 1·348 | 1·000 | 0·000 | — |
| 1·254 | 0·930 | 0·101 | −0·31 |
| 1·177 | 0·873 | 0·202 | −0·29 |
| 1·117 | 0·828 | 0·303 | −0·27 |
| 1·027 | 0·762 | 0·404 | −0·29 |
| | | Average = | −0·29 |
| 0·722 | 1·000 | 0·000 | — |
| 0·694 | 0·961 | 0·101 | −0·17 |
| 0·660 | 0·914 | 0·202 | −0·19 |
| 0·638 | 0·884 | 0·303 | −0·18 |
| 0·611 | 0·846 | 0·404 | −0·18 |
| | | Average = | −0·18 |

*Strontium chloride.*

| Acid concn. | $s/s_0$. | *c*. | *K*. |
|---|---|---|---|
| 1·292 | 1·000 | 0·000 | — |
| 1·214 | 0·940 | 0·104 | −0·20 |
| 1·129 | 0·874 | 0·356 | −0·17 |
| | | Average | −0·18 |
| 0·724 | 1·000 | 0·000 | — |
| 0·677 | 0·935 | 0·202 | −0·15 |
| 0·644 | 0·889 | 0·404 | −0·16 |
| | | Average = | −0·15 |

*Potassium chloride.*

| Acid concn. | $s/s_0$. | *c*. | *K*. |
|---|---|---|---|
| 1·368 | 1·000 | 0·000 | — |
| 1·323 | 0·967 | 0·101 | −0·14 |
| 1·275 | 0·932 | 0·202 | −0·15 |
| 1·248 | 0·912 | 0·276 | −0·14 |
| 1·203 | 0·879 | 0·404 | −0·14 |
| | | Average = | −0·14 |
| 0·724 | 1·000 | 0·000 | — |
| 0·715 | 0·987 | 0·101 | −0·06 |
| 0·692 | 0·955 | 0·202 | −0·10 |
| 0·667 | 0·920 | 0·404 | −0·09 |
| | | Average = | −0·08 |

*Lithium chloride.*

| Acid concn. | $s/s_0$. | *c*. | *K*. |
|---|---|---|---|
| 1·386 | 1·000 | 0·000 | — |
| 1·207 | 0·871 | 0·107 | −0·56 |
| 1·037 | 0·748 | 0·269 | −0·47 |
| 0·954 | 0·688 | 0·403 | −0·40 |
| | | Average = | −0·48 |
| 0·730 | 1·000 | 0·000 | — |
| 0·701 | 0·961 | 0·095 | −0·1[illegible] |
| 0·681 | 0·934 | 0·165 | −0·1[illegible] |
| 0·667 | 0·914 | 0·197 | −0·2[illegible] |
| 0·641 | 0·878 | 0·266 | −0·2[illegible] |
| | | Average = | −0·1[illegible] |

*Calcium chloride.*

(See p. 267.)

| Acid concn. | $s/s_0$. | *c*. | *K*. |
|---|---|---|---|
| 0·745 | 1·000 | 0·000 | — |
| 0·725 | 0·974 | 0·143 | −0·[illegible] |
| 0·712 | 0·957 | 0·221 | −0·[illegible] |
| 0·692 | 0·929 | 0·264 | −0·[illegible] |
| 0·665 | 0·893 | 0·327 | −0·[illegible] |
| 0·647 | 0·869 | 0·450 | −0·[illegible] |
| | | Average = | −0·[illegible] |

TABLE II (*contd.*)

*Magnesium chloride.*

| Acid | Acid concn. | $s/s_0$. | $c$. | $K$. |
|---|---|---|---|---|
| $r$ | 1·339 | 1·000 | 0·000 | — |
| $r$ | 1·106 | 0·826 | 0·285 | −0·29 |
| (+) | 0·709 | 1·000 | 0·000 | — |
| (+) | 0·644 | 0·909 | 0·216 | −0·19 |
| (+) | 0·589 | 0·830 | 0·411 | −0·20 |
| (+) | | | Average = | −0·19 |

*Cæsium nitrate.*

| Acid | Acid concn. | $s/s_0$. | $c$. | $K$. |
|---|---|---|---|---|
| $r$ | 1·402 | 1·000 | 0·000 | — |
| $r$ | 1·464 | 1·044 | 0·101 | 0·19 |
| $r$ | 1·567 | 1·118 | 0·202 | 0·24 |
| $r$ | 1·581 | 1·128 | 0·303 | 0·18 |
| $r$ | 1·670 | 1·191 | 0·404 | 0·19 |
| $r$ | | | Average = | 0·20 |
| (+) | 0·744 | 1·000 | 0·000 | — |
| (+) | 0·762 | 1·024 | 0·101 | 0·10 |
| (+) | 0·783 | 1·052 | 0·202 | 0·11 |
| (+) | 0·810 | 1·089 | 0·303 | 0·12 |
| (+) | 0·836 | 1·124 | 0·404 | 0·13 |
| (+) | | | Average = | 0·12 |

*Thallous nitrate.*

| Acid | Acid concn. | $s/s_0$. | $c$. | $K$. |
|---|---|---|---|---|
| $r$ | 1·430 | 1·000 | 0·000 | — |
| $r$ | 1·571 | 1·099 | 0·101 | 0·41 |
| $r$ | 1·674 | 1·170 | 0·202 | 0·34 |
| $r$ | 1·923 | 1·345 | 0·404 | 0·32 |
| $r$ | | | Average = | 0·36 |
| (+) | 0·758 | 1·000 | 0·000 | — |
| (+) | 0·804 | 1·061 | 0·101 | 0·25 |
| (+) | 0·858 | 1·132 | 0·202 | 0·27 |
| (+) | 0·951 | 1·255 | 0·404 | 0·24 |
| (+) | | | Average = | 0·25 |

*Rubidium nitrate.*

| Acid | Acid concn. | $s/s_0$. | $c$. | $K$. |
|---|---|---|---|---|
| $r$ | 1·382 | 1·000 | 0·000 | — |
| $r$ | 1·408 | 1·019 | 0·101 | 0·08 |
| $r$ | 1·431 | 1·035 | 0·202 | 0·08 |
| $r$ | 1·456 | 1·054 | 0·303 | 0·08 |
| $r$ | 1·490 | 1·076 | 0·404 | 0·08 |
| $r$ | | | Average = | 0·08 |
| (+) | 0·738 | 1·000 | 0·000 | — |
| (+) | 0·747 | 1·013 | 0·101 | 0·05 |
| (+) | 0·759 | 1·028 | 0·202 | 0·06 |
| (+) | 0·764 | 1·035 | 0·303 | 0·05 |
| (+) | 0·774 | 1·048 | 0·404 | 0·05 |
| (+) | | | Average = | 0·05 |

*Potassium nitrate.*

| Acid | Acid concn. | $s/s_0$. | $c$. | $K$. |
|---|---|---|---|---|
| $r$ | 1·373 | 1·000 | 0·000 | — |
| $r$ | 1·390 | 1·013 | 0·101 | 0·06 |
| $r$ | 1·408 | 1·025 | 0·202 | 0·05 |
| $r$ | 1·432 | 1·043 | 0·404 | 0·05 |
| $r$ | | | Average = | 0·05 |
| (+) | 0·732 | 1·000 | 0·000 | — |
| (+) | 0·735 | 1·005 | 0·101 | 0·02 |
| (+) | 0·738 | 1·009 | 0·202 | 0·02 |
| (+) | 0·740 | 1·011 | 0·404 | 0·01 |
| (+) | | | Average = | 0·02 |

*Ammonium nitrate.*

| Acid | Acid concn. | $s/s_0$. | $c$. | $K$. |
|---|---|---|---|---|
| $r$ | 1·380 | 1·000 | 0·000 | — |
| $r$ | 1·385 | 1·003 | 0·101 | 0·0 |
| $r$ | 1·385 | 1·003 | 0·202 | 0·0 |
| $r$ | 1·382 | 1·001 | 0·303 | 0·0 |
| $r$ | 1·370 | 0·991 | 0·404 | 0·0 |
| (+) | 0·730 | 1·000 | 0·000 | — |
| (+) | 0·731 | 1·000 | 0·101 | 0·0 |
| (+) | 0·729 | 1·000 | 0·202 | 0·0 |
| (+) | 0·733 | 1·000 | 0·303 | 0·0 |
| (+) | 0·733 | 1·000 | 0·404 | 0·0 |

*Sodium nitrate.*

| Acid | Acid concn. | $s/s_0$. | $c$. | $K$. |
|---|---|---|---|---|
| $r$ | 1·348 | 1·000 | 0·000 | — |
| $r$ | 1·324 | 0·983 | 0·101 | −0·08 |
| $r$ | 1·305 | 0·968 | 0·202 | −0·07 |
| $r$ | 1·236 | 0·917 | 0·404 | −0·09 |
| $r$ | | | Average = | −0·08 |
| (+) | 0·722 | 1·000 | 0·000 | — |
| (+) | 0·715 | 0·991 | 0·101 | −0·04 |
| (+) | 0·700 | 0·969 | 0·202 | −0·07 |
| (+) | 0·676 | 0·937 | 0·404 | −0·07 |
| (+) | | | Average = | −0·06 |

*Lithium nitrate.*

| Acid | Acid concn. | $s/s_0$. | $c$. | $K$. |
|---|---|---|---|---|
| $r$ | 1·342 | 1·000 | 0·000 | — |
| $r$ | 1·276 | 0·950 | 0·101 | −0·22 |
| $r$ | 1·227 | 0·915 | 0·202 | −0·19 |
| $r$ | 1·121 | 0·835 | 0·404 | −0·19 |
| $r$ | | | Average = | −0·20 |
| (+) | 0·722 | 1·000 | 0·000 | — |
| (+) | 0·707 | 0·978 | 0·101 | −0·09 |
| (+) | 0·688 | 0·953 | 0·202 | −0·10 |
| (+) | 0·652 | 0·903 | 0·404 | −0·11 |
| (+) | | | Average = | −0·10 |

The foregoing results are summarised in Table III, in which $a$ and $b$ represent the difference between the value of $K$ for the metal mandelate ($K_M$) and for its chloride ($K_{MCl}$) or nitrate respectively.

For the data of Table I, with certain of the metallic ions only a small range of concentrations of mandelic acid can be investigated, as acid salts are deposited at relatively low concentrations (see also original curves, *loc. cit.*). On this account the values of $K$ are not so constant as in the data of Table II, where a larger range of concentrations is available. In particular, with $r$-mandelic acid and calcium mandelate no values of $K$ can be calculated.

We may take $K_M$ as representing the salting-out effect of the metallic ion + compound formation (salting-in effect), and $K_{MCl}$ as denoting the joint salting-out effects of the metallic ion and of the chloride ion. The differences $a$ and $b$ will then represent the compound formation effect + the salting-out effect of the chloride and nitrate ion respectively, and will be independent of the salting-out effect of the metallic ion. Since the values obtained for $a$ and $b$ are approximately constant, we may conclude that the compound formation effect is independent of the metallic ion present. The effect of the metallic mandelates is therefore due to a combination of the mandelic acid with the mandelate ion of the types : HA,A′, 2HA,A′, and 3HA,A′, where A represents the mandelate ion.

It is generally agreed that the size of the ions determines the extent of the salting-out effect of a salt, and since potassium and chloride ions are approximately of the same size, we may assume, with Larsson (*loc. cit.*, 1931), that $K_{K^{\cdot}} = K_{Cl'}$. Since $K_{KCl} = -0{\cdot}14$,

TABLE III.

| | Mandelate. | Chloride. | Nitrate. | *a.* | *b.* |
|---|---|---|---|---|---|
| | | *Racemic acid.* | | | |
| Cs | 0·85 | 0·02 | 0·20 | 0·83 | 0·65 |
| Tl | 0·68 | — | 0·36 | — | 0·32 |
| Rb | 0·66 | −0·13 | 0·08 | 0·79 | 0·58 |
| K | 0·58 | −0·14 | 0·05 | 0·72 | 0·53 |
| $NH_4$ | 0·49 | −0·20 | 0·00 | 0·69 | 0·49 |
| Na | 0·34 | −0·29 | −0·08 | 0·63 | 0·42 |
| Li | 0·25 | −0·48 | −0·20 | 0·73 | 0·45 |
| Ba | 0·58 | −0·14 | — | 0·72 | — |
| Sr | 0·43 | −0·18 | — | 0·61 | — |
| Mg | 0·18 | −0·29 | — | 0·47 | — |
| | | | Average = | 0·69 | 0·49 |
| | | *Active acid.* | | | |
| Tl | 0·47 | — | 0·25 | — | 0·22 |
| Cs | 0·30 | 0·02 | 0·12 | 0·28 | 0·18 |
| Rb | 0·28 | −0·06 | 0·03 | 0·34 | 0·23 |
| K | 0·27 | −0·08 | 0·02 | 0·35 | 0·25 |
| $NH_4$ | 0·25 | −0·09 | 0·00 | 0·34 | 0·25 |
| Na | 0·22 | −0·18 | −0·06 | 0·40 | 0·28 |
| Li | 0·09 | −0·19 | −0·10 | 0·28 | 0·19 |
| Sr | 0·26 | −0·15 | — | 0·41 | — |
| Ba | 0·25 | −0·15 | — | 0·40 | — |
| Ca | 0·20 | −0·12 | — | 0·32 | — |
| Mg | 0·08 | −0·19 | — | 0·27 | — |
| | | | Average = | 0·34 | 0·23 |

then $K_{K^{\cdot}} = K_{Cl'} = -0{\cdot}07$ for the racemic acid, and $K_{KCl} = -0{\cdot}08$, giving $K_{K^{\cdot}} = K_{Cl'} = -0{\cdot}04$ for the active acid. The constant derived from the results of salting-out with metallic chlorides, representing the extent of compound formation for all the metallic mandelates, will then be $K = 0{\cdot}69 + (-0{\cdot}07) = 0{\cdot}62$, and for the active acid $K = 0{\cdot}34 + (-0{\cdot}04) = 0{\cdot}30$. Taking the values of $K$ for potassium nitrate $= +0{\cdot}05$ and $+0{\cdot}02$ for the *r*- and the (+)-acid respectively, we get $K_{NO_3'} = +0{\cdot}12$ and $+0{\cdot}06$. The corresponding values of $K$ representing the extent of compound formation for all the metallic mandelates are therefore $K = 0{\cdot}49 + 0{\cdot}12 = 0{\cdot}61$, and $K = 0{\cdot}23 + 0{\cdot}06 = 0{\cdot}2?$ respectively. The values of $K$ for compound formation after correction are therefor in both cases in close agreement. These results indicate that there is a marked difference in the extent of compound formation between the racemic acid and its salts, and between the active acid and its salts, the former being twice as great as the latter.

If we calculate the solubility of the acid for different concentrations of salt from th equation $Kc = \log s/s_0$, using $K = 0{\cdot}62$ and $s_0 = 1{\cdot}335$ for the racemic acid, and $K = 0{\cdot}3$ and $s_0 = 0{\cdot}738$ for the active acid, we get the following results :

| | | | | | |
|---|---|---|---|---|---|
| Racemic acid : | $s$ | 1·54 | 1·77 | 2·05 | 2·36 |
| | $c$ | 0·1 | 0·2 | 0·3 | 0·4 |
| Active acid : | $s$ | 0·79 | 0·84 | 0·90 | 0·96 |
| | $c$ | 0·1 | 0·2 | 0·3 | 0·4 |

If in the case of the racemic acid we calculate the value of $s - 3c$, which is equal to tl concentration of free acid on the assumption that the 3 : 1 acid salt is formed in solution, v get the values 1·24, 1·17, 1·15, and 1·16 respectively, giving a fairly constant value for tl concentration of free acid in the solution. Similarly for the active acid we may calcula the value of $s - c$ on the assumption that the 1 : 1 acid salt is found in solution, a obtain the values 0·69, 0·64, 0·60, and 0·56. It would appear, therefore, that with the and the active acid the 3 : 1 and the 1 : 1 acid salts respectively are formed to a mark extent in solution. Some support for this conclusion is derived from the fact that the 3 acid salts are common with racemic acid, but have not been isolated with the active aci

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## 53. *Simultaneous Adsorption from Dilute Aqueous Solutions.*

By W. J. Jones, R. A. Hudson, and J. T. Jones.

The object of this investigation was to determine, in certain cases, the relative adsorbability of two different solutes from a solution containing both. It has been found that for certain of the investigated systems, the curve relating adsorption to equilibrium concentration is inflected, and this appears to be the first reported instance of such curves with pairs of substances in dilute solution. In all cases investigated, a mutual displacement effect is apparent.

At the concentrations employed, it was found that Traube's rule was obeyed in the adsorption of acetone, of methyl ethyl ketone, and of methyl *n*-propyl ketone from aqueous solution.

Adsorption from some binary liquid systems has been found to give **S**-shaped isothermals (Flörow, *Kolloid-Z.*, 1925, **36**, 215; Pawlow, *ibid.*, p. 217; Ostwald and Schulze, *ibid.*, p. 289; Bartell and Sloan, *J. Amer. Chem. Soc.*, 1929, **51**, 1637, 1643; Bartell, Scheffler, and Sloan, *ibid.*, 1931, **53**, 2501; Rao, *J. Physical Chem.*, 1932, **36**, 616). In the present work, isothermals of the same shape have been obtained with ternary systems consisting of dilute aqueous solutions containing phenol and a ketone, or aniline and a ketone, the adsorbent being sugar-charcoal. Since, in the present experiments, the concentration of a solute never exceeds 0·50 g.-mol./l., the adsorption of the water may probably be regarded as constant. The equation of Markham and Benton (*J. Amer. Chem. Soc.*, 1931, **53**, 503), if applicable to the present systems, would give, for a given equilibrium concentration of ketone, a hyperbolic isothermal for the adsorption of the phenol or aniline; however, the isothermals obtained are not of this form.

### Experimental.

All the substances used were carefully purified before use. The adsorbent was one uniform sample of finely powdered sugar-charcoal, which had been quartered, thoroughly mixed, dried at 130° for 12 hours, and thereafter preserved in a vacuum desiccator over calcium chloride; the ash from 5 g. was not weighable. Phenol was estimated by the Landolt–Koppeschaar method (*Ber.*, 1871, **4**, 770; *Z. anal. Chem.*, 1876, **15**, 233), aniline by that of Vaubel (*J. pr. Chem.*, 1877, **15**, 237), and acetone by that of Messinger (*Ber.*, 1888, **21**, 3366); in estimations of methyl ethyl ketone and methyl *n*-propyl ketone, it was found necessary to use 2N-alkali with 20 minutes' standing. In solutions containing both phenol and ketone, the former was removed as *s*-tribromophenol before estimation of the ketone; aniline was likewise removed as *s*-tribromoaniline.

Each system was prepared by taking 1·000 g. of the charcoal and 100·0 c.c. of standard aqueous solution in a sealed bottle, which was then immersed in a thermostat at 25·0° and agitated until equilibrium had been attained. After about 20 hours, an aliquot portion of the supernatant liquid, free from charcoal, was removed for analysis.

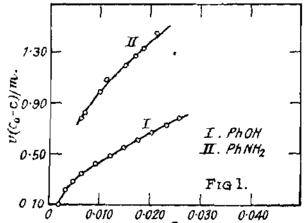
That true equilibrium had been established was proved by trial experiments in which the time of agitation was varied. It was found that, with the same initial concentration of ketone and of phenol or aniline, the same eqnilibrium concentrations were obtained in whichever order the solutions were added to the charcoal or whether both ketone and phenol or aniline were added together in the same solution.

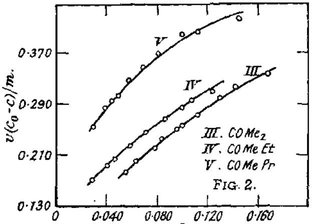
The results obtained for the adsorption of phenol from its dilute aqueous solution are shown in Fig. 1, wherein $v(c_0 - c)/m$ is plotted against $c$, $c_0$ being the initial concentration in g.-mol./l. of the phenol or aniline in the solution used in the experiment, and $c$ its equilibrium concentration, when $v$ c.c. of solution are treated with $m$ g. of adsorbent. The adsorption of aniline is similarly represented in Fig. 1, and that of each of the ketones in Fig. 2, which thus conform with Traube's rule (*Annalen*, 1891, **265**, 27). It has been considered unnecessary to tabulate the results obtained, since, owing to the nature of sugar-charcoal, they could not be exactly reproduced except with the sample here used.

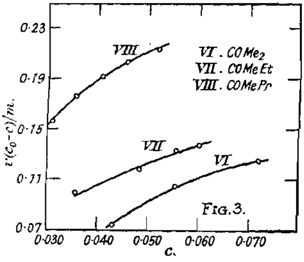
The adsorptions, $v(c_0 - c)/m$, are respectively represented closely by the following functions at the concentrations used in the experiments:

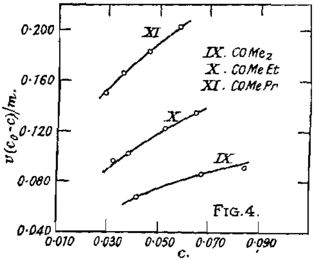
Phenol, $6{\cdot}25\, c^{0{\cdot}57}$ Aniline, $9{\cdot}09\, c^{0{\cdot}48}$
Acetone, $0{\cdot}955\, c^{0{\cdot}66}$ Methyl *n*-propyl ketone, $0{\cdot}922\, c^{0{\cdot}36}$
Methyl ethyl ketone, $0{\cdot}745\, c^{0{\cdot}43}$

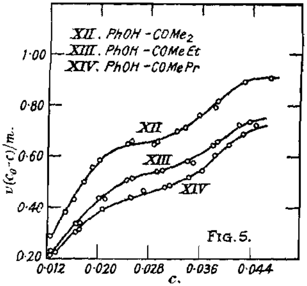
The adsorption of the ketones from solutions containing also phenol at initial concentration 0·0530 g.-mol./l. is shown in Fig. 3, and that of the ketones from ketone–aniline solutions, wherein the aniline was initially at concentration 0·0496, in Fig. 4. In both these figures, $c_0$ and $c$ refer to the ketone concentration. It will be noted that these curves are not S-shaped.

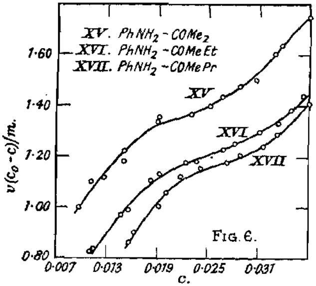



The adsorption of phenol from phenol–ketone solutions containing the ketone initially concentration 0·217 g.-mol./l. is represented in Fig. 5, and of aniline from aniline–ketc solutions of initial ketone concentration 0·206 in Fig. 6.

That the adsorption of the ketones is depressed by phenol or aniline is seen on compar: Fig. 3 or Fig. 4 respectively with Fig. 2. Likewise, the depressing effect of ketone on t adsorption of phenol or aniline is shown by a comparison of Fig. 5 or Fig. 6 with Fig. 1. T

S-shape of curves XII—XVII may be variously explained, *e.g.*, by the assumption that the adsorbed substances combine together, or that an additional layer is formed on an originally unimolecular layer, but the present experiments do not permit of decision in this respect.

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# 54. *The Extent of Dissociation of Salts in Water. Part V. Calcium Mandelate.*

By Cecil W. Davies.

Calcium mandelate has been studied in dilute aqueous solution at 25°. The electrical conductivity is abnormally low, and leads to the conclusion that the intermediate ion, $C_6H_5\cdot CH(OH)\cdot CO_2Ca^{\cdot}$ is present in considerable amounts; in 0·005M-solution 15% of the calcium is in this form. A value $K = 0{\cdot}035$ is derived for the dissociation constant of the intermediate ion, and this is used to calculate the ionic composition of certain solutions, containing sodium *l*-mandelate in the presence of calcium salts, which Levene and Rothen have found to exhibit abnormal optical activity. The calculations lead to a consistent value for the molecular rotation of the calcium mandelate ion differing greatly from that of the free mandelate ion, a fact which suggests that the constituents of the intermediate ion are united by a definite chemical linkage.

Some years ago Levene and Rothen (*J. Physical Chem.*, 1930, **34**, 2567) reported the effect of a large number of salts on the optical activity of sodium *l*-mandelate in aqueous solution. Although in most cases the usual small " salt effect " was observed, yet solutions containing the alkaline-earth metals, and especially calcium, showed very much greater changes. The authors considered that their results proved the complete dissociation of calcium and barium mandelate in dilute aqueous solution, but actnally the evidence was inconclusive, and, on the contrary, these anomalous salt effects seemed too great to be due to normal electrostatic influences, and to imply a more intimate interaction between the mandelate ion and the added cation. To test this, the conductivity of calcium mandelate was measured.

The calcium mandelate, prepared from calcium carbonate and mandelic acid, was obtained as anhydrous crystals on addition of alcohol to the aqueous solution. After three recrystallisations by the same method the salt was dried in a vacuum at 50° for 24 hours, and its purity was confirmed by conductimetric titration against sodium oxalate. The salt forms soft waxy crystals which are not wetted by water and for this reason dissolve extremely slowly. During the recrystallisations this inconvenience was overcome by first moistening the dry crystals with a drop of alcohol; after this treatment they sank in water and dissolved readily.

The conductivity apparatus and technique were as described in a former paper (J., 1937, 432), measurements being made at 1000 and 3150 cycles. The solutions were made up by weight, and their equivalent concentrations were calculated from the molecular weight $M = 342{\cdot}20$ and the following density figures, which were determined in these laboratories by Dr. W. H. Banks: $m$ 0·0119, $d$ 0·9985; $m$ 0·0215, $d$ 0·9997. All measurements were made at 25° ± 0·005°, and are based on the Jones and Bradshaw standard (*J. Amer. Chem. Soc.*, 1933, **55**, 1780).

The results are in Table I, where col. 1 gives the equivalent concentration, and col. 2 the equivalent conductivity obtained by applying the normal solvent correction, *i.e.*, by subtracting

Table I.

| $C \times 10^4$. | Λ, norm. | Λ, corr. | Λ, calc. | $100 \times (1 - \alpha)$. | $I$. | $K$. |
|---|---|---|---|---|---|---|
| 7·2235 | 83·08 | 83·30 | 84·50 | 2·1 | 0·001069 | 0·0289 |
| 10·370 | 81·96 | 82·14 | 83·71 | $2{\cdot}8_5$ | 0·001525 | 0·0294 |
| 17·786 | 80·05 | 80·17 | 82·15 | 3·8 | 0·002600 | 0·0355 |
| 24·513 | 78·49 | 78·57 | 81·10 | 4·9 | 0·003558 | 0·0361 |
| 34·715 | 76·52 | 76·56 | 79·81 | 6·68 | 0·004976 | 0·0350 |
| 39·730 | 75·66 | 75·70 | 79·29 | 7·35 | 0·005668 | 0·0353 |
| 49·798 | 74·11 | 74·14 | 78·33 | 8·80 | 0·007032 | 0·0350 |
| 57·362 | 73·04 | 73·05 | 77·72 | 9·70 | 0·008048 | 0·0353 |
| 81·109 | 70·20 | 70·21 | 76·01 | 12·4 | 0·01117 | 0·0354 |
| 121·98 | 66·33 | 66·34 | 73·87 | 16·6 | 0·01628 | 0·0346 |

the conductivity of the solvent from that of the solution. It has been shown in earlier papers that these results will be too low, whilst figures corrected for hydrolysis on the assumption that the sole impurity in the water is carbon dioxide will be slightly too high. The corrected figures given in col. 3 were obtained by adding to those of col. 2 two-thirds of the difference between these and the hydrolysis-corrected values (cf. Banks and Davies, this vol., p. 73); the uncertainty introduced by this procedure is very small except for the two most dilute solutions.

When plotted against the square root of the equivalent concentration, the conductivities give an almost straight line up to $C = 0{\cdot}01$, *i.e.*, far beyond the limits of validity of Onsager's equation; this behaviour is abnormal for an aqueous salt solution, but has frequently been found for incompletely dissociated salts in non-aqueous solvents. Moreover, with increasing concentration they become increasingly lower than the values to be expected for a completely dissociated salt. These values are shown in col. 4, calculated from the empirical extension of Onsager's equation derived in a previous paper (Righellato and Davies, *Trans. Faraday Soc.*, 1930, **26**, 592), which for calcium mandelate takes the form $\Lambda$, calc. $= 88{\cdot}85 - 161\, f_{12}(C)$; here the value for zero concentration, 88·85, is the sum of the mobilities of the mandelate ion, 29·40 (Banks and Davies, *loc. cit.*), and of the calcium ion, 59·45 (Shedlovsky and Brown, *J. Amer. Chem. Soc.*, 1934, **56**, 1066). A comparison of cols. 4 and 3 shows that the discrepancy is already large for the first three points, which are approximately within the range of validity of Onsager's limiting equation, and at 0·01N. the measured conductivity is too low by 10%. We believe that this is due to the formation of the intermediate ion according to the scheme $Ca^{\cdot\cdot} + C_6H_5{\cdot}CH(OH){\cdot}CO_2' \rightleftharpoons C_6H_5{\cdot}CH(OH){\cdot}CO_2Ca^{\cdot}$; the further association to form the neutral salt is likely to be negligible at the concentrations considered. The figures given in col. 5 of Table I show the percentages of calcium in the form of the intermediate ion, calculated by the method of the previous paper (Righellato and Davies, *loc. cit.*), and on the assumption that the mobility of the intermediate ion at zero concentration is 30. The value of this constant is necessarily uncertain; if its value had been taken as 25, the figures obtained for $(1 - \alpha)$, the fraction associated, would have been approximately 5% lower than those shown. Col. 6 of the table shows the ionic strength, calculated from the formula $I = (1 + 2\alpha)m$, where $m$ is the molar concentration, and col. 7 gives the dissociation constant calculated from the relation $\log K = \log \{Ca^{\cdot\cdot}\}\{M'\}/\{CaM^{\cdot}\} = \log \alpha(1 + \alpha)m/(1 - \alpha) - 2{\cdot}02\sqrt{I} + BI$; the adjustable constant $B$ was found graphically to have the value 2·7. With the exception of the most dilute measurements, for which the solvent-corrected conductivities are uncertain, the constancy of $K$ leaves nothing to be desired; for the last six points the mean value is 0·0351 and the maximum deviation from this value corresponds to an error in the measured conductivity of 0·05 unit. On the other hand, inaccuracies in the empirical equation on which the calculations are based, and in the value taken for the mobility of the intermediate ion, may introduce errors of 5% or more, so that the value $K = 0{\cdot}035$ may be in error by 0·002. The behaviour of calcium mandelate is in marked contrast with that of the commoner calcium salts, which are usually regarded as typically strong electrolytes. It is also noteworthy that calcium mandelate is much weaker than the barium salt, for which a dissociation constant $K = 0{\cdot}17$ has been derived (Banks and Davies, *loc. cit.*).

It is now possible to calculate the ionic composition of the solutions investigated by Levene and Rothen, if we assume that the same dissociation constant will apply to the calcium salts of the active and inactive acids. Levene and Rothen made three series of measurements. In the first, varying amounts of calcium hydroxide were added to *l*-mandelic acid; four measurements of this type were available, the data being read from Fig. 1 of the authors' paper. In the second series, various amounts of calcium chloride were added to sodium mandelate; only one of these measurements could be used, since the second referred to a mixture of ionic strength greater than 1, in which the concentration o[f] the calcium mandelate cation could not be even approximately calculated. In the thir[d] series calcium chloride was added to mandelic acid in the presence of hydrochloric acid and these measurements were also unsuitable for our purpose since calculation showed tha[t] less than 0·5% of the mandelate radical was united to calcium. The results of the calcu[l]ations are given in Table II. Col. 1 shows the stoicheiometric concentration of mandel[ate]

TABLE II.

| $C_1$. | $C_2$. | $[M]_D^{25°}$. | [Ca˙˙]. | [M′]. | [CaM˙]. | [OH′]. | [CaOH˙]. | $[M_{CaM˙}]_D^{25°}$. |
|---|---|---|---|---|---|---|---|---|
| | | | | *Mandelic acid + calcium hydroxide.* | | | | |
| 0·0098 | 0·0049 | 183·6° | 0·0042 | 0·0091 | 0·0007 | — | — | 274° |
| 0·0098 | 0·0190 | 194·2 | 0·0132 | 0·0082 | 0·0016 | 0·0240 | 0·0042 | 286 |
| 0·0174 | 0·0174 | 192·8 | 0·0123 | 0·0148 | 0·0026 | 0·0149 | 0·0025 | 284 |
| 0·0260 | 0·0130 | 189·0 | 0·0097 | 0·0227 | 0·0033 | — | — | 273 |
| | | | | *Sodium mandelate + calcium chloride.* | | | | |
| 0·04983 | 0·0292 | 193·14 | 0·0196 | 0·04023 | 0·0096 | — | — | 263 |

acid or sodium mandelate, col. 2 that of calcium hydroxide or calcium chloride, col. 3 the molecular rotation for the solution. The next five columns show the concentrations of the individual species, that of the calcium mandelate ion being calculated from the equation given above, and that of the calcium hydroxide ion in the alkaline solutions from the equation $\log [Ca^{··}][OH'] / [CaOH^{·}] = \log 0{\cdot}031 + 2{\cdot}02\sqrt{I} - 2I$ (Kilde, *Z. anorg. Chem.*, **1934**, **218**, 113; and see following papers). The last column shows the molecular rotation of the calcium mandelate ion calculated from the formula of the simple mixture rule, $2[M] = (1 + \alpha)[M_{mand.}] + (1 - \alpha)[M_{CaM}]$, where $[M_{mand.}]$, the molecular rotation of the free mandelate ion, is given the value determined by Levene and Rothen, *viz.*, 176·7. This treatment assumes that the whole change in rotation is due to the appearance of the new ionic species with its own characteristic optical activity; it neglects the "normal" salt effect, due to the influence exerted by the neighbouring free ions, a procedure justified, as a close approximation, by the very small effects found by Levene and Rothen for normal salts.

The dissociation constant of barium mandelate is also known (Banks and Davies, *loc. cit.*), and the same treatment has been applied to the two most dilute of Levene and Rothen's solutions containing barinm ion. The results are as follows:

| $C_1$. | $C_2$. | $[M]_D^{20°}$. | [Ba˙˙]. | [M′]. | [BaM˙]. | $[M_{BaM˙}]_D^{25°}$. |
|---|---|---|---|---|---|---|
| | | | *Mandelic acid + barium hydroxide.* | | | |
| 0·05 | 0·0256 | 179·95° | 0·0227 | 0·0471 | 0·0029 | 233° |
| | | | *Sodium mandelate + barium chloride.* | | | |
| 0·04983 | 0·044 | 181·92 | 0·0393 | 0·04513 | 0·0047 | 232 |

For both the calcium mandelate and the barium mandelate ion the calculated molecular rotations are constant within the error of experiment and calculation. Here, then, as with the other properties of salt solutions so far investigated, the incomplete dissociation theory provides a consistent explanation of apparently anomalous results.

The molecular rotations now known for mandelic acid and its derivatives are: acid, 237·3°; free ion, 176·7°; barium mandelate ion, 233°; calcinm mandelate ion, 276°. The association of a mandelate ion with a calcium ion is therefore accompanied by a considerably greater change in optical activity than is the formation of the un-ionised acid. This fact, like the abnormally low dissociation constant, is evidence that the process cannot be described in terms of a purely electrostatic linkage. The structure of the calcinm mandelate ion is further discussed in the following papers.

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## 55. *The Conductivity of Calcium Iodate and its Solubility in Salt Solutions.*

By WILLIAM C. A. WISE and CECIL W. DAVIES.

The conductivity of calcium iodate in water has been measured at 18°. The results show that the salt, like other iodates, can be regarded as incompletely dissociated, and a value $K = 0{\cdot}13$ is derived for the dissociation constant of the intermediate ion $CaIO_3^{·}$. Determinations have also been made of the solubility of the salt in water and numerous salt solutions at 25°. The solubility is very markedly dependent on the

nature of the added salt, but corrections for incomplete dissociation remove the anomalies and give values for the mean ionic activity coefficient which lie approximately on a common curve. The measurements in sodium mandelate solutions confirm the dissociation constant of calcium mandelate reported in the preceding paper.

In pursuance of previous work (see J., 1935, 1416) the solubility of calcium iodate hexahydrate has been measured in a number of salt solutions at 25°. In the interpretation of the results, conductivity data for the pure iodate were required, and these were obtained by measurements at 18°.

The salt was prepared by dropwise addition of solutions of potassium iodate and calcium chloride in equivalent amounts to a large volume of conductivity water. The crystalline hexahydrate separated, and was washed first by decantation and then in the solubility tubes until a constant solubility was attained. In the calculations the value 389·9 has been used for the molecular weight of the anhydrous salt. The solubility measurements were at 25° ± 0·01° and were carried out in the same way as the measurements on barium iodate (Macdougall and Davies, J., 1935, 1416), except that weighed samples were taken for analysis, and the densities of the saturated solutions were determined. The conductivity measurements, at 18° ± 0·005°, were carried out as described in earlier papers (see J., 1937, 432), readings being taken at two frequencies, 1000 and 3150. The more concentrated solutions were prepared by weight dilution of an almost saturated stock solution the concentration of which was determined by analysis, and the more dilute solutions by addition of stock solution from a weight burette to conductivity water in the cell. For the more concentrated solutions the relative density could not be taken as unity, and was assumed to be the same at 18° as at 25°.

The conductivity results, based on the Jones and Bradshaw standard, are given in Table I; line 1 shows the equivalent concentration, $C$, and line 2 the equivalent conductivity, after subtraction of the conductivity of the solvent. At the higher concentrations the conductivity is abnormally low, and the method of the preceding paper was used to calculate $(1 - \alpha)$, the fraction of calcium in the form of the intermediate ion, $CaIO_3^{\cdot}$; the results are in line 3. In the calculations the equivalent conductivity of calcium iodate at zero concentration was taken to be 85·24; this is the value given by the sum of Kohlrausch's mobilities (see Davies, "Conductivity of Solutions," 2nd Edn., p. 205), reduced by 0·09% to correct to the Jones and Bradshaw standard (J., 1937, 1326), and it is also consistent with our measurements in the most dilute solutions. For the mobility of the calcium iodate ion the value 34·0 was adopted.

Table I.

*The conductivity of calcium iodate at 18°.*

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| $C \times 10^4$ ... | 2·000 | 2·633 | 4·279 | 5·876 | 8·852 | 11·693 | 38·77 | 52·94 | 58·15 | 81·85 |
| $\Lambda$ ........... | 83·20 | 82·83 | 82·42 | 81·67 | 80·88 | 80·28 | 76·44 | 74·95 | 74·43 | 72·73 |
| $100 (1 - \alpha)$ | — | — | — | — | — | — | $1·9_5$ | $2·7_7$ | $3·1_3$ | $3·9_0$ |
| $10^4 . I$ ...... | — | — | — | — | — | — | 57·40 | 77·93 | 85·40 | 119·6 |
| $10^2 . \sqrt{I}$ ... | — | — | — | — | — | — | 7·580 | 8·828 | 9·241 | 10·94 |
| $K$ ........... | — | — | — | — | — | — | 0·140 | 0·126 | 0·121 | 0·126 |

Lines 4 and 5 of the table give the ionic strength and its square root, and line 6 th dissociation constant of the calcium iodate ion, calculated from the relation :

$$\log K = \log \alpha (1 + \alpha)m/(1 - \alpha) - 2·02 \sqrt{I} + 2I$$

The results are satisfactorily constant, and the value $K = 0·13$ is adopted.

The results of the solubility measurements are illustrated in the figure and given i Table II, in which col. 1 gives the concentration of the solvent salt and col. 3 the solubilit of calcium iodate, both in millimols./l., and col. 2 gives the density of the solution. Whe a comparison is possible, the results are generally in good agreement with the determi ations of Kilde (*Z. anorg. Chem.*, 1934, **218**, 113), the two values for the salt in water bei identical; but for the solubilities in calcium chloride Kilde's results, whilst agreeing wi ours in the most dilute solution and also at 0·05M-calcium chloride, are higher at 0·025 both values at this concentration are shown in the table. We have not checked our val

TABLE II.

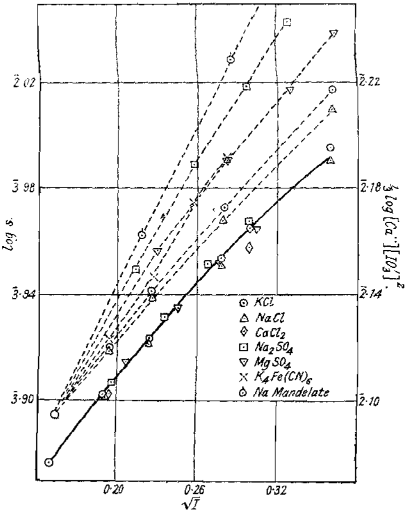
| *m.* | $d^{25^\circ}_{4^\circ}$. | *s.* | [$CaIO_3$·]. | | | | *I.* | $\frac{1}{3}$ log [Ca··][$IO_3$']² | $f_{\pm}$. | Δ. |
|---|---|---|---|---|---|---|---|---|---|---|
| Water. | | | | | | | | | | |
| — | 0·9998 | 7·840 | 0·479 | — | — | — | 0·02257 | $\bar{2}$·0769 | 0·742 | −0·003 |
| Sodium chloride solutions. | | | | [$NaIO_3$]. | | | | | | |
| 12·5 | 1·0010 | 8·285 | 0·472 | 0·047 | — | — | 0·03686 | $\bar{2}$·1012 | 0·702 | +0·003 |
| 25·0 | 1·0015 | 8·676 | 0·476 | 0·093 | — | — | 0·04998 | $\bar{2}$·1211 | 0·670 | +0·001 |
| 50·0 | 1·0025 | 9·287 | 0·482 | 0·187 | — | — | 0·07671 | $\bar{2}$·1502 | 0·627 | +0·003 |
| 100·0 | 1·0050 | 10·23 | 0·507 | 0·382 | — | — | 0·1293 | $\bar{2}$·1903 | 0·572 | ±0·000 |
| Potassium chloride solutions. | | | | [$KIO_3$]. | | | | | | |
| 12·5 | 1·0008 | 8·312 | 0·476 | 0·070 | — | — | 0·03642 | $\bar{2}$·1022 | 0·700 | ±0·000 |
| 25·0 | 1·0017 | 8·730 | 0·480 | 0·140 | — | — | 0·05009 | $\bar{2}$·1231 | 0·667 | −0·001 |
| 50·0 | 1·0032 | 9·387 | 0·490 | 0·282 | — | — | 0·07690 | $\bar{2}$·1533 | 0·622 | −0·002 |
| 100·0 | 1·0057 | 10·42 | 0·521 | 0·577 | — | — | 0·1296 | $\bar{2}$·1955 | 0·565 | −0·007 |
| Calcium chloride solutions. | | | | | | | | | | |
| 6·25 | 1·0001 | 6·692 | 0·591 | — | — | — | 0·03765 | $\bar{2}$·1019 | 0·701 | +0·004 |
| 25·0 | 1·0016 | 5·414 | 0·868 | — | — | — | 0·08959 | $\bar{2}$·1570 | 0·616 | +0·007 |
| 25·0 | — | 5·57* | 0·88 | — | — | — | 0·8994 | $\bar{2}$·1649 | 0·606 | −0·002 |
| 50·0 | 1·0036 | 4·900 | 1·177 | — | — | — | 0·1623 | $\bar{2}$·2005 | 0·558 | +0·007 |
| Sodium sulphate solutions. | | | | [$NaIO_3$]. | [$CaSO_4$]. | [$NaSO_4$']. | | | | |
| 6·25 | 1·001 | 8·898 | 0·451 | 0·049 | 1·445 | 0·132 | 0·03845 | $\bar{2}$·1071 | 0·692 | −0·002 |
| 12·5 | 1·002 | 9·745 | 0·440 | 0·102 | 2·397 | 0·475 | 0·05523 | $\bar{2}$·1315 | 0·655 | −0·003 |
| 18·75 | 1·003 | 10·45 | 0·436 | 0·157 | 3·127 | 0·970 | 0·07215 | $\bar{2}$·1512 | 0·626 | −0·005 |
| 25·0 | 1·004 | 11·05 | 0·428 | 0·213 | 3·724 | 1·586 | 0·08916 | $\bar{2}$·1673 | 0·603 | −0·006 |
| Magnesium sulphate solutions. | | | | [$MgIO_3$·]. | [$CaSO_4$]. | [$MgSO_4$]. | | | | |
| 6·25 | 1·001 | 9·038 | 0·459 | 0·253 | 1·281 | 0·772 | 0·04248 | $\bar{2}$·1141 | 0·681 | −0·003 |
| 12·5 | 1·002 | 9·788 | 0·446 | 0·481 | 2·044 | 2·292 | 0·06017 | $\bar{2}$·1349 | 0·649 | ±0·000 |
| 18·75 | 1·004 | 10·42 | 0·443 | 0·707 | 2·623 | 4·167 | 0·07680 | $\bar{2}$·1517 | 0·625 | +0·001 |
| 25·0 | 1·004 | 10·95 | 0·441 | 0·936 | 3·104 | 6·275 | 0·09256 | $\bar{2}$·1647 | 0·606 | +0·001 |
| *Potassium ferrocyanide solutions.* | | | | | | | | | | |
| 1·25 | 1·0007 | 8·377 | — | — | — | — | — | — | — | — |
| 2·5 | 1·0013 | 8·839 | — | — | — | — | — | — | — | — |
| 3·75 | 1·0018 | 9·430 | — | — | — | — | — | — | — | — |
| 5·0 | 1·0023 | 9·804 | — | — | — | — | — | — | — | — |
| Sodium mandelate solutions. | | | | [$NaIO_3$]. | [CaM·]. | | | | *K.* | |
| 20·0 | 1·0002 | 9·177 | 0·440 | 0·081 | 1·902 | — | 0·04277 | $\bar{2}$·1124 | 0·033 | |
| 50·0 | 1·0047 | 10·69 | 0·420 | 0·218 | 3·765 | — | 0·07348 | $\bar{2}$·1490 | 0·036 | |
| 100·0 | 1·0090 | 12·83 | 0·396 | 0·486 | 6·506 | — | 0·1242 | $\bar{2}$·1870 | 0·036 | |

* Kilde's determination (*loc. cit.*).

as our collaboration ended before Kilde's paper appeared, but we think that probably it is low; a possible explanation is that the time required to effect saturation is much longer in solutions containing a common ion, and that for this measurement saturation had not been attained.

If now we assume all the salts concerned to be completely dissociated and apply the conventional treatment to our results, we have (except for the calcium chloride series where the presence of the common ion modifies the formula) $4\gamma^3 s^3 = S_0$, where $\gamma$ is the mean (stoicheiometric) activity coefficient, $s$ the solubility, and $S_0$ the solubility product. The relation can be written as log $s$ = const. − log $\gamma$, and a graph of log $s$ against the square root of the ionic strength will show whether the changes in log $\gamma$ are consistent with the Debye–Hückel activity theory. The curves shown by broken lines in the figure illustrate this treatment. The solubilities depend to a far greater extent than would have been expected on the nature of the added salt, the deviations of one from another being most marked even at the lowest concentrations. So far as the results in sodium and magnesium sulphates are concerned, the anomalies fall into line with those observed by Brönsted and LaMer many years ago (cf. Brönsted and Petersen, *J. Amer. Chem. Soc.*, 1921, **43**, 2265; LaMer and Cook, *ibid.*, 1929, **51**, 2622) and characterised by them as "The Electric Type Effect," or "The Unsymmetrical Valence Type Effect." But the striking feature of the present measurements is that the greatest anomaly is found with the uni-univalent salt sodium mandelate, which actually affects the solubility of calcium iodate more than twice as much as sodium or potassium chloride of the same concentration. It

will be shown below that this anomaly is quantitatively explained by corrections for ion-association, just as the " Unsymmetrical Valence Type Effect " was accounted for in an earlier paper (J., 1930, 2421).




To make allowance for ion association, the compositions of the solutions must b calculated in terms of the actual concentrations of the ions and non-conducting molecule present in each. This has been done for the measurements in the chloride and sulphat solutions by using equations of the form $\log [XY] = \log [X][Y] - \log K - A\sqrt{I} + BI$ where [XY] is the concentration of a non-conducting molecule or intermediate ion, an the values of the constants $K$, $A$, and $B$, taken from this or earlier papers, are :

| | $CaIO_3^{\cdot}$. | $NaIO_3$. | $KIO_3$. | $MgIO_3^{\cdot}$. | $CaSO_4$. | $MgSO_4$. | $NaSO_4'$. |
|---|---|---|---|---|---|---|---|
| $K$ .............. | 0·13 | 3·0 | 2·0 | 0·19 | 0·0053 | 0·0063 | 0·20 |
| $A$ .............. | 2·02 | 1·01 | 1·01 | 2·02 | 4·04 | 4·04 | 2·02 |
| $B$ .............. | 2·0 | 1·0 | 1·0 | 2·6 | 4·0 | 4·0 | 1·3 |

The chlorides were assumed to be completely dissociated. Similar calculations for tl potassium ferrocyanide series are precluded by lack of data. Approximate calculatioı (*J. Amer. Chem. Soc.*, 1937, **59**, 1760) make it probable that the solutions investigatı contain considerable amounts of the ions $KFe(CN)_6'''$ and $K_2Fe(CN)_6''$, and the presen in varying amounts of these, together with the products of their association with calciu ions, may account for the unusual shape of the uncorrected curve.

The results of the calculations are given in cols. 4—7 of Table II, which show t concentrations in millimols. of the products of association; the concentrations of the otł ionic species can be found by subtraction, and hence the ionic strength shown in col. We can now apply the solubility product principle in its accurate form, $f_{\pm}^3[Ca^{\cdot\cdot}][IO'_3]^2 =$ where $f_{\pm}$ is the mean ionic activity coefficient, and in place of the expression $\log s =$ const log $\gamma$ we have $\frac{1}{3} \log [Ca^{\cdot\cdot}][IO'_3]^2 =$ const. $- \log f_{\pm}$. Values of the term on the left-hı side of this expression are given in col. 9 of the table, and are plotted against the sqı

root of the ionic strength in the lower series of points (right-hand scale of co-ordinates) in the figure.

It will be seen that the corrections remove the large anomalies in every case, and the points all lie close to a common curve. The determination of activity coefficients from these results involves an extrapolation of the curve to zero ionic strength, and this, on account of the relatively high solubility of calcium iodate, is somewhat uncertain. Use can here be made of the earlier results with barium iodate (Macdougall and Davies, *loc. cit.*). These, as would be expected on theoretical grounds, can by a transposition of scale be accurately superimposed on the corrected calcium iodate results; and as they extend down to an ionic strength of 0·0025, at which the limiting Debye–Hückel equation is valid, the extrapolation presents no difficulty. The extrapolated value for the solubility product is $6{\cdot}953 \times 10^{-7}$, and from this the mean ionic activity coefficients shown in col. 10 of the table are obtained. Col. 11 shows the deviation $\Delta = f_{\pm \text{expt.}} - f_{\pm \text{equ.}}$, where the latter values are obtained from the empirical equation $-\log f_{\pm} = 1{\cdot}01\sqrt{I}/(1 + \sqrt{I}) - 0{\cdot}19I$. This form of equation, suggested by Dr. E. A. Guggenheim, is valid at higher ionic strengths than the Brönsted equation, $-\log f_{\pm} = 1{\cdot}01\sqrt{I} - BI$, used in previous papers from this laboratory. The agreement is good, and below an ionic strength of 0·1, at any rate, there is no consistent increase in the deviation with increasing ionic strength; this suggests that the deviations are no greater than the errors of experiment and calculation.

For the measurements in sodium mandelate solutions this equation was used to calculate values of $\frac{1}{3}\log [Ca^{\bullet\bullet}][IO_3']^2$, and hence the amount of calcium mandelate necessarily present was obtained by successive approximations; allowance for the calcium iodate cation was made as before, whilst sodium mandelate is known to be completely dissociated (Banks and Davies, this vol., p. 73). The results are in the table, where the last column now shows the dissociation constant of calcium mandelate calculated from the equation $\log K = \log [Ca^{\bullet\bullet}][M']/[CaM^{\bullet}] - 2{\cdot}02\sqrt{I} + 2{\cdot}7I$ (cf. preceding paper). The values are satisfactorily constant, and agree with the figure $K = 0{\cdot}035$ obtained in the preceding paper by an entirely different method.

Battersea Polytechnic, London, S.W. 11. [*Received, January 24th, 1938.*]

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## 56. *The Extent of Dissociation of Salts in Water. Part VI. Some Calcium Salts of Organic Acids.*

By Cecil W. Davies.

Calcium lactate and mandelate are known to be abnormally weak electrolytes, and the purpose of the present work was to investigate the structural factors on which this anomaly depends. The dissociation constants of several calcium salts of monobasic acids have been obtained, and of these the weakest is the glycollate; in a 0·02M-solution of this salt only one-half of the calcium is in the form of free calcium ions. Amongst other calcium salts of oxy-acids, the methoxyacetate and pyruvate are weak, though not as weak as the salts of α-hydroxy-acids; the salts of β-hydroxy-acids are stronger. The aminoacetate has almost the same dissociation constant as the lactate, showing that the anomaly is not restricted to oxy-acids.

In the two preceding papers it has been shown that calcium mandelate is a relatively weak electrolyte, and Kilde (*Z. anorg. Chem.*, 1936, **229**, 321) has found the same to be true of calcium lactate. The results reported in this paper form part of an investigation into the structural factors on which the anomaly depends. The method used was to measure the solubility of calcium iodate in the presence of the sodium salt of an organic acid; the dissociation constant of the calcium salt of the acid was then calculated by the method applied to calcium mandelate in the preceding paper. In addition, Kilde's results, which are not strictly comparable with ours, have been recalculated, and some measurements of the conductivity of calcium acetate have also been considered.

*The Dissociation Constant of Calcium Lactate.*—The value $K = 0\cdot04$ was obtained by Kilde (*loc. cit.*) by methods generally similar to those used here and in the preceding paper; *i.e.*, he measured the solubility of calcium iodate in the presence of sodium or calcium lactate, and calculated the amount of the calcium lactate ion necessarily present to bring the results into harmony with those for normal salts; by plotting log [Ca˙˙][Lac.′]/[CaLac.˙] − $2\cdot02\sqrt{I}$ against $I$ (where $I$ is the ionic strength) he then obtained the result log [Ca˙˙][Lac.′]/[CaLac.˙] − $2\cdot02\sqrt{I} + 2\cdot8I = 0\cdot04$. Kilde, however, made no corrections for the presence of sodium iodate molecules and $CaIO_3^{\cdot}$ ions, which he assumed to be completely dissociated. As we have evidence that this is not so, and as the corresponding corrections, though not affecting Kilde's main conclusions, are nevertheless significant when we come to compare the dissociation constant of calcium lactate with those of other salts of hydroxy-acids, we have recalculated the results on the same basis as our other figures. The results are in Table I. Cols. 1 and 2 show Kilde's values for the concentration of solvent salt and the solubility of calcium iodate, both in millimols./l. The next six columns give the results of the calculations; the figures in col. 5 are derived from $\frac{1}{3}$ log $[Ca^{\cdot\cdot}][IO_3']^2 = \bar{3}\cdot9474 + 1\cdot01\sqrt{I}/(1 + \sqrt{I}) - 0\cdot19I$, an equation which follows from the results of the preceding paper; col. 7 gives the calculated concentration of the CaLac.˙ ion, and col. 8 the dissociation constant of this ion, calculated from the equation log $K$ = log [Ca˙˙][Lac.′]/[CaLac.˙] − $2\cdot02\sqrt{I} + 2\cdot8I$. The last column shows the dissociation constant obtained by Kilde's method.

TABLE I.

*Solubility of Calcium Iodate in Lactate Solutions.*

| *m.* | *s.* | $[NaIO_3]$. | $[CaIO_3^{\cdot}]$. | $\frac{1}{3}$ log $[Ca^{\cdot\cdot}][IO_3']^2$. | *I.* | [CaLac.˙]. | *K.* | $K_{Kilde}$. |
|---|---|---|---|---|---|---|---|---|
| | | | | Sodium lactate solutions. | | | | |
| 200·0 | 16·89 | 1·19 | 0·36 | $\bar{2}$·2298 | 0·2257 | 11·82 | 0·035 | 0·042 |
| 100·0 | 13·15 | 0·49 | 0·38 | $\bar{2}$·1868 | 0·1239 | 7·15 | 0·032 | 0·040 |
| 40·0 | 10·32 | 0·17 | 0·41 | $\bar{2}$·1381 | 0·06305 | 3·46 | 0·032 | 0·044 |
| 20·0 | 9·18 | 0·08 | 0·44 | $\bar{2}$·1124 | 0·04274 | 1·92 | 0·033 | 0·047 |
| 10·0 | 8·53 | 0·04 | 0·46 | $\bar{2}$·0958 | 0·03264 | 1·00 | 0·034 | 0·047 |
| | | | | Calcium lactate solutions. | | | | |
| 99·2 | 5·85 | — | 1·01 | $\bar{2}$·2149 | 0·1820 | 65·46 | 0·035 | 0·039 |
| 49·6 | 5·93 | — | 0·85 | $\bar{2}$·1799 | 0·1127 | 26·10 | 0·035 | 0·040 |
| 19·8 | 6·33 | — | 0·69 | $\bar{2}$·1371 | 0·06211 | 7·45 | 0·036 | 0·049 |
| 9·92 | 6·77 | — | 0·60 | $\bar{2}$·1123 | 0·04263 | 3·12 | 0·035 | 0·049 |
| 4·96 | 7·15 | — | 0·54 | $\bar{2}$·0955 | 0·03257 | 1·35 | 0·035 | 0·053 |

*The Dissociation Constant of Calcium Hydroxide.*—This has also been determined by Kilde, and, as with calcium lactate, it seemed desirable to make the recalculations. The results are in Table II, where col. 1 gives the added electrolyte and its concentration in millimols./l. The $K$ values are calculated from the equation log $K$ = log [Ca˙˙][OH′]/[CaOH˙] − $2\cdot02\sqrt{I} + 2I$

TABLE II.

*Solubility of Calcium Iodate in Alkaline Solutions.*

| *m.* | | *s.* | $[NaIO_3]$. | $[CaIO_3^{\cdot}]$. | $\frac{1}{3}$ log $[Ca^{\cdot\cdot}][IO_3']^2$. | *I.* | [CaOH˙]. | *K.* | $K_{Kilde}$. |
|---|---|---|---|---|---|---|---|---|---|
| 10·0 | NaOH | 8·4 | 0·04 | 0·47 | $\bar{2}$·0965 | 0·0331 | 0·59 | (0·058) | (0·20) |
| 25·0 | NaOH | 9·4 | 0·10 | 0·44 | $\bar{2}$·1199 | 0·0480 | 2·09 | 0·034 | 0·048 |
| 25·0<br>100·0 | NaOH<br>NaCl | 11·4 | 0·52 | 0·47 | $\bar{2}$·2019 | 0·1523 | 2·45 | 0·026 | 0·047 |
| 50·0 | NaOH | 10·5 | 0·21 | 0·42 | $\bar{2}$·1491 | 0·0738 | 4·23 | 0·029 | 0·053 |
| 50·0<br>50·0 | NaOH<br>NaCl | 11·4 | 0·43 | 0·44 | $\bar{2}$·1883 | 0·1263 | 3·32 | 0·037 | 0·056 |
| 10·8 | $Ca(OH)_2$ | 6·4 | — | 0·65 | $\bar{2}$·1202 | 0·0483 | 1·00 | (0·14) | (0·26) |
| 10·8<br>100·0 | $Ca(OH)_2$<br>NaCl | 8·5 | 0·31 | 0·63 | $\bar{2}$·2009 | 0·1501 | 3·13 | 0·030 | 0·056 |
| | | | | | | | Mean | 0·031 | |

*The Dissociation Constant of Calcium Acetate.*—At low concentrations MacGregory's co ductivity data (Landolt–Börnstein Tabellen, 5te Aufl., 1081) for calcium acetate at 18° are fair agreement with Onsager's equation. At the higher concentrations the experimental valu are somewhat lower than values calculated from the empirical extension of Onsager's equati for a completely dissociated salt (*Trans. Faraday Soc.*, 1930, **26**, 592), and the method of calc

ation used by Righellato and Davies (*ibid.*) leads to the following values for the dissociation constant: $C = 0{\cdot}03$, $K = 1{\cdot}0$; $C = 0{\cdot}05$, $K = 0{\cdot}9$; $C = 0{\cdot}1$, $K = 1{\cdot}0$; mean: $K = 1{\cdot}0$. The accuracy of this value is not great, but the consistency of the results is sufficiently good to show that calcium acetate is a stronger electrolyte than calcium nitrate, and that at the concentrations considered in this series of papers its dissociation into free ions is almost complete.

*New Solubility Measurements.*—These were made as described in the previous paper, except that the saturated solutions were estimated, with little apparent sacrifice of accuracy, by the ordinary volumetric methods. Each measurement reported is the mean of two titrations, agreeing within at least 0·2%, between which the saturated solution was passed for a second time through the saturating column. The solubility in pure water was checked before and after each series with a given salt. The results are at 25° ± 0·01°.

An approximately 1N-sodium hydroxide solution was prepared from washed "AnalaR" sticks, and stored in a nickel reservoir; it was standardised by titration against weighed samples of "AnalaR" potassium hydrogen tartrate and potassium hydrogen phthalate. With one exception the sodium salt solutions were made up from this solution and solutions of the purified acids, an added drop of phenolphthalein being just decolourised. The salicylic, glycollic, and cyanoacetic acids were commercial samples; their acid equivalents agreed within 0·1% with the theoretical values. The glycine, an "AnalaR" sample, was also used without further purification. The pyruvic acid (b. p. 73°/11 mm.) was redistilled just before use; its acid equivalent was 87·5 (Calc.: 88·0). The methoxyacetic acid was prepared in these laboratories, b. p. 102°/18 mm.; its acid equivalent was 90·2 (Calc.: 90·05). The sodium β-hydroxybutyrate solutions were made up by weight from a sample of the salt which had been recrystallised from absolute alcohol and dried in a vacuum.

Before each salt solution was taken into use, a portion was mixed with 25 ml. of an almost saturated solution of calcium iodate, and the whole titrated, under standard conditions, after standing for one hour. Only with the β-hydroxybutyrate was there any evidence of interaction; for this salt a small correction (+ 0·3%) was derived, and was applied to the subsequent results.

The results are given in Table III in the same manner as before; col. 7 shows the calculated concentration of the product of association of the calcium ion with the organic anion present, and col. 8 shows the dissociation constant of this ion, calculated from the equation $\log K = \log [Ca^{\cdot\cdot}][X'] / [CaX^{\cdot}] - 2{\cdot}02\sqrt{I} + 2{\cdot}8I$. The adjustable constant in this equation has been given the value 2·8 in view of the values previously found for similarly constituted ions: calcium mandelate, 2·7 (cf. preceding papers); barium mandelate, 2·83 (Banks and Davies, this vol., p. 73); calcium lactate, 2·8 (Kilde, *loc. cit.*). It will undoubtedly apply with the required accuracy to the data of Table III.

The results for sodium aminoacetate are probably less accurate than the others, as no special precautions were taken to protect the alkaline solutions from the atmosphere. The calculations, also, for this salt were complicated by the necessity of allowing for the $CaOH^{\cdot}$ ion formed in these alkaline solutions, and for hydrolysis; in obtaining the figures shown in the table (HX represents glycine) the acid dissociation constant of glycine was taken to be $3{\cdot}4 \times 10^{-10}$, and it was assumed that the glycine molecules do not contribute to the ionic strength.

The calculations for calcium lactate in Table I reveal some points of interest. A comparison of the last two columns shows that the chief effect of the recalculations is to reduce the dissociation constant. The constancy of the new values is very satisfactory, the mean of the measurements being 0·034, with an average deviation of ± 0·001. Kilde's results, on the other hand, show variations at the lower concentrations, which are more pronounced in the calcium lactate than in the sodium lactate series. Kilde neglected these, no doubt correctly, in deriving his mean value, $0{\cdot}04_0$, but it is satisfactory to find that the discrepancies are entirely removed by the new method of calculation; the fact provides additional evidence for the substantial accuracy of the dissociation constants assigned to sodium and calcium iodates. In Table II, where the same considerations are involved, the recalculation greatly reduces, though it does not entirely remove, the anomalies in the most dilute solutions.

Another striking feature of the figures in Table I is the constancy of $K$ in the two most concentrated solutions, in which two-thirds or more of the total calcium is in the form of calcium lactate ion. With the glycollates, oxalates, and other relatively weak salts of the transitional metals it is found (Ferrell, Ridgion, and Riley, J., 1934, 1440; Money and Davies, *ibid.*, p. 400) that as the concentration rises the cation shows a marked tendency

TABLE III.

| *m.* | s. | $[NaIO_3]$. | $[CaIO_3^{\cdot}]$. | $\frac{1}{3}\log[Ca^{\cdot\cdot}][IO_3']^2$. | *I.* | $[CaX^{\cdot}]$. | *K.* |
|---|---|---|---|---|---|---|---|
| | | | | Sodium glycollate. | | | |
| 40·0 | 10·56 | 0·176 | 0·404 | $\bar{2}$·1378 | 0·06267 | 4·017 | 0·0257 |
| 20·0 | 9·315 | 0·082 | 0·429 | $\bar{2}$·1118 | 0·04242 | 2·294 | 0·0257 |
| | | | | Sodium methoxyacetate. | | | |
| 40·0 | 9·664 | 0·160 | 0·446 | $\bar{2}$·1396 | 0·06447 | 1·733 | 0·077 |
| 20·0 | 8·850 | 0·078 | 0·455 | $\bar{2}$·1138 | 0·04367 | 0·948 | 0·075 |
| | | | | Sodium pyruvate. | | | |
| 40·0 | 9·609 | 0·159 | 0·449 | $\bar{2}$·1399 | 0·06463 | 1·568 | 0·086 |
| 20·0 | 8·837 | 0·077 | 0·456 | $\bar{2}$·1139 | 0·04371 | 0·904 | 0·079 |
| | | | | Sodium β-hydroxybutyrate. | | | |
| 43·04 | 9·470 | 0·166 | 0·461 | $\bar{2}$·1439 | 0·06850 | 0·953 | 0·16 |
| 21·48 | 8·791 | 0·088 | 0·462 | $\bar{2}$·1164 | 0·04561 | 0·620 | 0·13 |
| | | | | Sodium salicylate. | | | |
| 40·0 | 9·241 | 0·152 | 0·468 | $\bar{2}$·1409 | 0·06567 | 0·480 | 0·31 |
| 20·0 | 8·652 | 0·076 | 0·468 | $\bar{2}$·1146 | 0·04429 | 0·328 | 0·24 |
| | | | | Sodium aminoacetate. | | | |
| 40·0 | 10·01 | 0·166 | 0·429 | $\bar{2}$·1388 | 0·06373 | 2·571 | 0·045 |
| | (The solution also contained : $[CaOH^{\cdot}]$, 0·082; $[HX]$, 1·086; $[OH']$, 1·00.) | | | | | | |
| 20·0 | 9·113 | 0·080 | 0·439 | $\bar{2}$·1127 | 0·04292 | 1·665 | 0·038 |
| | (The solution also contained : $[CaOH^{\cdot}]$, 0·064; $[HX]$, 0·756; $[OH']$, 0·69.) | | | | | | |
| | | | | Sodium cyanoacetate. | | | |
| 40·0 | 9·241 | 0·152 | 0·468 | $\bar{2}$·1409 | 0·06567 | 0·480 | 0·31 |
| 20·0 | 8·652 | 0·076 | 0·468 | $\bar{2}$·1146 | 0·04429 | 0·328 | 0·24 |

to associate with an increasing number of anions, to form first neutral molecules and then complex anions. If calcium lactate exhibited similar behaviour it would be shown in a change of $K$ at the higher concentrations. It is true that this might possibly be masked by a compensation of errors, since the ionic strength of the most concentrated solutions of Table I is beyond the range in which our equations have been tested; but it appears more probable that the calcium lactate ion has no great tendency to undergo further association even in the presence of a large excess of lactate ions.

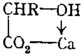
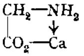
The values now available for the dissociation constants of calcium salts of univalent organic acids are as follows :

| | | | | | |
|---|---|---|---|---|---|
| Glycollate | 0·026 | Methoxyacetate | 0·076 | Salicylate | 0·28 |
| Lactate | 0·034 | Pyruvate | 0·083 | Cyanoacetate | 0·28 |
| Mandelate | 0·035 | β-Hydroxybutyrate | 0·15 | Acetate | 1·0 |
| Aminoacetate | 0·042 | | | | |

It is hardly necessary to point out that these figures show no relation to the dissociation constants of the corresponding acids.

The weakest of the salts is the glycollate. A 0·02M-solution of this will contain only one-half of its calcium in the form of free calcium ions, whilst at higher concentrations the salt will probably exist mainly in the uni-univalent ionised form $(CaX)^{\cdot}X'$. The other α-hydroxy-acid salts are almost as weak, and it is natural to suggest that a possible chelate structure, (I), contributes in all three cases to the stability of the intermediate ion. The effect is not confined to the salts of α-hydroxy-acids; it is still present, though much diminished, in the methoxyacetate and pyruvate. In the β-hydroxybutyrate, salicylate, and cyanoacetate, where chelation would result in a six-membered ring, it is interesting to find that the effect is much more feeble, if it exists at all; these three salts have higher dissociation constants than has calcium iodate. Finally, the result for the aminoacetate shows that the influence of an α-nitrogen atom is comparable with that of an α-oxygen atom in causing an abnormally low dissociation constant. The measurements cannot be interpreted with quite as much confidence in this case, since in addition to the $CaOH^{\cdot}$ ion and

the undissociated glycine, for which approximate allowance was made, there are conceivably present the species $Ca(OH)\cdot CO_2\cdot CH_2\cdot NH_2$ and $[Ca(OH)\cdot CO_2\cdot CH_2\cdot NH_3]^{\cdot}$. Probably, however, association will lead primarily to (II), and in alkaline solutions at moderate concentrations the calcium salts of the common amino-acids will exist mainly in such a form.

(I.)   (II.)

This work was carried out, and the two preceding papers prepared for publication, during the tenure of a Leverhulme research fellowship. The author is indebted also to Dr. J. Keuyon, F.R.S., for his active interest in the work, and kindness in providing the pure pyruvic and methoxyacetic acids.

Battersea Polytechnic, London, S.W. 11. [*Received, January 24th*, 1938.]

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# NOTES.

## *Occurrence of Kaempferol in* Crocus. By J. R. Price, (Mrs.) G. M. Robinson, and Robert Robinson.

Flowers of *Crocus* species, for which we are greatly indebted to Dr. E. J. Collins, were immersed in 1% hydrochloric acid in order to extract the anthocyanins, which proved to be diglycosides of delphinidin in most cases, although the pigments of two species were found to be derived from malvidin. After 2—3 weeks the solutions in contact with *Crocus asturicus* flowers (two varieties) deposited very pale yellow crystals, which were also obtained from *Crocus speciosus* and from two or three other species in lesser relative amount.

The precipitates were collected, the aqueous acid solutions extracted with ethyl acetate, and the residue after removal of the solvent triturated with a few drops of acetic acid, leaving a yellow powder, which was added to the precipitated material. The substance crystallised readily from acetic acid in pale yellow needles, which became intensely yellow on exposure to the air. A dye-trial on cotton mordanted with aluminium, iron, and a mixture of the two gave results identical with those furnished by synthetic kaempferol. The yellow solution in concentrated sulphuric acid exhibited a green fluorescence, and this gradually changed to an intense bright blue fluorescence. The ferric reaction in alcoholic solution was also identical with that of kaempferol.

The substance, crystallised only once, had m. p. 272—274° (lit., 276—277°) and for further identification was converted into the acetate by refluxing with an excess of acetic anhydride and a few drops of pyridine for 2 hours. Most of the acetic anhydride was removed by distillation under diminished pressure, bot methyl alcohol was added, and the solution at once filtered. On cooling, colourless needles separated and these were collected, washed with methyl alcohol, and dried in a vacuum over sulphuric acid (Found: C, 58·6; H, 4·9; $CH_3\cdot CO$, 36·0; loss at 110° in a high vacuum, 6·5. Found in material so dried: C, 61·2; H, 4·1. $C_{23}H_{18}O_{10},CH_4O$ requires C, 59·3; H, 4·5; $4CH_3\cdot CO$, 35·5%. Calc. for $C_{23}H_{18}O_{10}$: C, 60·8; H, 4·0%). This specimen softened at 116°, was fluid at 120°, resolidified as the temperature rose to 140°, and then had m. p. 179—180°.

Exactly the same behaviour of tetra-acetylkaempferol crystallised from methyl alcohol has been described by Perkin and Wilkinson (J., 1902, **81**, 587), but these authors stated definitely that no loss of weight occurs during the preliminary fusion. This may well be true if the heating to 120° is not prolonged and is carried out under the atmospheric pressure. The above experiment shows clearly, however, that the phenomenon is due to solvation. Recrystallisation from ethyl alcohol, with distillation of one third of the solvent in order to remove methyl alcohol, afforded colourless needles, m. p. 182° alone or mixed witb authentic synthetic tetra-acetylkaempferol (Robinson and Shinoda, J., 1925, **127**, 1980).

Only a few flowers were used in these experiments, so, although not more than 100 mg. of kaempferol were isolated, the petals of *Crocus asturicus* must be comparatively rich in flavonol content. The kaempferol is probably present as such in a dispersed form, possibly in co-pigment combination with the anthocyanin, the less favoured alternative being the occurrence of a

saccharide which is hydrolysed with quite unusual ease by means of cold 1% hydrochloric acid.—DYSON PERRINS LABORATORY, OXFORD UNIVERSITY, and THE JOHN INNES HORTICULTURAL INSTITUTION. [*Received, December 10th,* 1937.]

*The Mercuric Halides of Dimethyl Telluride.* By FREDERICK CARR and T. G. PEARSON.

THE alkyl derivatives of metals in the form of their mercuric halides have been frequently used in the identification of free radicals, and for such a purpose we have synthesised the dimethyl telluride compounds by mixing cold solutions of the mercuric halides and dimethyl telluride in dry acetone. The double compounds, $TeMe_2,HgX_2$, are rapidly and quantitatively formed and, being almost insoluble, may be separated from the acetone by filtration, as far as possible out of contact with air, recrystallised from suitable solvents, and dried in a vacuum. They are almost odourless when pure, but hydrolyse rapidly in air to liberate the abominable persistent odour of dimethyl telluride. To avoid handling them, their compositions were ascertained by comparing the weights of the mercuric chloride, bromide, and iodide derivatives obtained from aliquot portions of a standard solution of dimethyl telluride in acetone by the addition of excess of the appropriate mercuric halide dissolved in acetone.

*Dimethyl telluride mercuric chloride,* $Te(CH_3)_2,HgCl_2$, formed colourless, microscopic, square and hexagonal plates, m. p. 179° (decomp.). *Dimethyl telluride mercuric bromide,* $Te(CH_3)_2,HgBr_2$, formed colourless or very pale cream-coloured, minute crystals, which appear as hexagonal rhombs or squares under the microscope, showing strong polarisation colours; m. p. 160—161° (decomp.). It separated from alcohol or benzene in fine needles, m. p. 158°, slightly soluble in methyl iodide, chloroform, and ether. *Dimethyl telluride mercuric iodide,* $Te(CH_3)_2,HgI_2$, formed canary-yellow, vitreous, columnar crystals, showing strong polarisation; m. p. 107° (slight decomp.); from alcohol or benzene, it separated in paler golden-yellow needles, m. p. 108° (slight decomp.). All three compounds were recrystallised from acetone.—IMPERIAL COLLEGE, LONDON, S.W. 7. [*Received, January 25th,* 1938.]

## 57. *Constituents of the Leaves of Certain* Leucadendron *Species. Part I. Leucodrin.*

By WILLIAM SAGE RAPSON.

Leucodrin has been isolated from the leaves of *Leucadendron concinnum*, *L. adscendens*, and *L. Stokoei*, and a preliminary study of its constitution made. It is a dilactone, $C_{15}H_{16}O_8$, containing one phenolic and three alcoholic hydroxyl groups. The phenolic hydroxyl is present in a *p*-hydroxyphenylethyl group. *Dibromoleucodrin* and *dichloroleucodrin* show unexpected properties. Both are dilactones containing one acidic group (titration experiments) and three reactive hydrogen atoms (Zerewitinow test). They would be expected, therefore, to give diacyl derivatives. Actually, tetra-acyl derivatives $C_{15}H_{10}O_8X_2Ac_4$ (X = Cl or Br) are obtained, in which the acidic properties of the original compounds have disappeared.

Rutin has been identified as a further constituent of the above *Leucadendron* species, having been isolated in large amounts from *L. Stokoei.*

LEUCODRIN was first isolated from the leaves of *L. concinnum* by Meiring-Beck (*Pharm. J.*, 1886, **17**, 327, 408), and later by Schuchardt (*ibid.*, p. 755), by Merck (*Merck's Ber.*, 1895, 3), and by Hesse (*Annalen*, 1896, **290**, 314). Besides leucodrin Merck isolated a glycoside leucoglycodrin from *L. concinnum*, but no other constituents of the leaves were reported. Both these substances are very bitter, and their presence in the leaf is probably responsible for the use of extracts of the leaves as a quinine substitute in the past (cf. Watt and Breyer-Brandwijk, "The Medicinal and Poisonous Plants of Southern Africa," Edinburgh, 1932). For the present work, leucodrin was obtained from the leaves of three species of *Leucadendron*—from *L. concinnum*, *L. adscendens*, and *L. Stokoei.*

Little information with regard to its chemical structure came from the experiments of Hesse and Merck on leucodrin (*loc. cit.*). Merck favoured a formulation $C_{15}H_{16}O_8$

with eight hydroxyl groups (formation of an octa-acetyl derivative), and Hesse from later experiments stated that leucodrin had the formula $C_{16}H_{20}O_9$ and gave a triacetyl derivative. The analyses and molecular-weight determinations presented here indicate the formula $C_{15}H_{16}O_8$. Titration experiments establish the presence of two lactone groups in the molecule; this is confirmed by the preparation of the corresponding *dihydroxydiamide*, *dihydroxybisethylamide*, and *dihydroxybisbenzylamide*. Of the remaining four oxygen atoms, Zerewitinow estimations indicate that three are in hydroxyl groups. Evidence for the presence of a fourth hydroxyl group, however, comes from two directions. First, acetylation of leucodrin yields a crystalline acetyl leucodrin, and the repeated acetyl determinations on this compound (C and H values are not significant) indicate that it is a *tetra-acetyl leucodrin*. Propionylation, butyrylation, and benzoylation experiments under various conditions all fail to yield crystalline products; mixtures of products may result. Secondly, leucodrin condenses with acetone to yield an iso*propylidene leucodrin* which gives a *diacetyl* iso*propylidene leucodrin* on acetylation, and yields two molecules of methane with the Grignard reagent; thus indicating the original presence of four hydroxyl groups.

These results are confirmed by the study of *leucodrin methyl ether* and *bromoleucodrin methyl ether*. The methyl ether is formed from leucodrin by carefully controlled treatment with diazomethane and is oxidised by potassium permanganate to give anisic acid. It contains two lactone groups, and the Zerewitinow test reveals the presence of two hydroxyl groups. An iso*propylidene-leucodrin methyl ether*, however, still gives a *mono-acetyl* derivative and yields one molecule of methane with the Grignard reagent. Bromoleucodrin methyl ether is formed by the direct action of bromine on leucodrin methyl ether. It is oxidised by potassium permanganate to 3-bromoanisic acid and contains two lactone groups and two reactive hydrogen atoms. Its iso*propylidene* derivative, however, also yields one molecule of methane with the Grignard reagent. Both of these compounds resemble leucodrin itself in failing to give crystalline acyl derivatives—in these cases even the product of acetylation fails to crystallise.

Leucodrin is extremely stable to the action of both acids and alkalis. Boiling concentrated hydrochloric acid has no action on it, and even after vigorous treatment with 15% sodium hydroxide solution it can be regenerated unchanged on acidification of the mixture. Hesse (*loc. cit.*) reported as one of the properties of leucodrin that it gave a yellow coloration with alkali. Completely purified leucodrin, however, gives no colour with alkali, the colour reaction of the crude material being due to traces of the flavonol glycoside rutin, which can be obtained in quantity from the leaves of *L. Stokoei*.

Potash fusion of leucodrin yields a mixture of *p*-hydroxybenzoic acid, acetic acid, and β-*p*-hydroxyphenylpropionic acid. The first two result from the last on potash fusion, so the presence of the skeleton (*p*) $OH{\cdot}C_6H_4{\cdot}CH_2{\cdot}CH_2{\cdot}C$ in the leucodrin molecule is all that can be deduced. Alkaline solutions of leucodrin couple with diazonium salts, and with bromine leucodrin yields a *dibromoleucodrin*, $C_{15}H_{14}O_8Br_2$. The latter reaction proceeds quantitatively, and titration of leucodrin with bromide–bromate mixture provides the most accurate method of determining its molecular weight. The product of the methylation of dibromoleucodrin with diazomethane is oxidised to 3 : 5-dibromoanisic acid by potassium permanganate. Dibromoleucodrin, however, possesses unexpected properties. From titration experiments it contains one acidic and two lactone groups. The acidic group cannot be esterified catalytically. Zerewitinow estimations indicate the presence of three reactive hydrogen atoms. Since one of these is in the acidic group, we should expect to obtain diacyl derivatives on acylation. But dibromoleucodrin yields *tetra-acetyl* and *tetrapropionyl dibromoleucodrins*, $C_{15}H_{10}O_8Br_2(COR)_4$ ($R = CH_3$ and $CH_2{\cdot}CH_3$), which are no longer acidic; the acidic group disappears during acylation. Both compounds, however, are hydrolysed to dibromoleucodrin by alkalis. This series of changes is confirmed by the study of *dichloroleucodrin* and *tetra-acetyl dichloroleucodrin*, which possess corresponding properties.

Attempts to obtain degradation products by the action of nitric acid have not been successful; the only crystalline product isolated gives analytical figures corresponding to a *dinitroleucodrin*, $C_{15}H_{14}O_8(NO_2)_2$. It is soluble in sodium bicarbonate solution. Further degradation experiments are in progress.

## Experimental.

*Extraction of Leucodrin.*—The leaves were dried, ground, and extracted continuously with hot alcohol till free from bitter material. The alcohol was then evaporated from the extract, the residue dissolved in water, and the solution clarified by the addition of lead subacetate solution. On evaporation of the clear filtrate from the lead precipitation, the leucodrin crystallised. In some cases a yellow flocculent precipitate separated from the clear solution if this was kept for 24 hours before evaporation. In such cases a fairly clear separation of the yellow material from the leucodrin could be obtained by cooling the dilute aqueous solution, and filtering off the pigment before evaporation in a vacuum. The final viscous mother-liquor after the crystallisation of the leucodrin contained sugars which yielded phenylglucosazone on treatment with phenylhydrazine in the usual way. By this procedure, *L. concinnum* (female plant) yielded 16% as leucodrin, besides traces of pigment; *L. adscendens* (female plant) yielded 20% as leucodrin, and appreciable amounts of pigment; and *L. Stokoei* (female plant) yielded 16% as leucodrin and 10% as pigment (all the yields are calculated on the dry weight of the leaf). Slight variations in the yields depended on the sex of the plant and the season of the year at which the specimen was collected. In no case was any attempt made to isolate the glycoside leucoglycodrin.

*Identification of the Yellow Pigment as Rutin.*—As obtained by the above procedure, the yellow material consisted of a mass of interlaced crystals which was very retentive of water on the filter. The mass was dried, powdered, and dissolved in a large quantity of ethyl alcohol, the excess of which was evaporated once solution had been achieved. From the concentrated solution, after treatment with decolorising charcoal, the pigment separated in a crystalline form easy to filter. When pure, the crystals coalesced to opaque droplets in the melting point tube at 184°, and these did not clear till 193°. Even on prolonged heating no meniscus formed (Found: C, 48·5, 48·4; H, 5·6, 5·4; loss in weight at 160°, 8·5. Calc. for $C_{27}H_{30}O_{16},3H_2O$: C, 48·7; H, 5·4; $H_2O$, 8·1%). That it was a glycoside of quercitin was indicated by the production of phloroglucinol and protocatechuic acid on potash fusion, and this was confirmed by its quantitative hydrolysis (cf. Smith, J., 1898, **73**, 699) to yield quercetin (Found: quercetin, 45·0. Calc. for $C_{27}H_{36}O_{19}$: quercetin, 45·5%). Its probable identity with rutin was established by the isolation (cf. Perkin, J., 1910, **97**, 1776) of the phenylosazones of glucose and rhamnose from the hydrolysis mixture. As the osazone of rhamnose was difficult to obtain pure, the rhamnose itself was isolated by the method adopted by Perkin (*loc. cit.*). To make certain of this identity, a sample of the substance was treated with excess of diazomethane (Attree and Perkin, J., 1927, 238) and from the hydrolysis of the product a substance with the same characteristics as 5 : 7 : 3′ : 4′-tetramethyl quercetin was isolated.

*Leucodrin.*—Leucodrin, recrystallised from water, formed elongated prisms of rectangular outline, m. p. 212—212·5°. It gave no coloration with ferric chloride and when completely freed from pigment it gave no yellow colour with acid or alkali. It was sparingly soluble in non-hydroxylic solvents except dioxan and ethyl acetate, and crystallised unchanged from boiling concentrated hydrochloric acid [Found: C, 55·6, 55·6; H, 4·9, 5·2; *M* (Rast), 376 OMe, nil; reactive H (Zerewitinow estimation in pyridine), 0·87, 0·92. Calc. for $C_{15}H_{16}O$ (three reactive hydrogens): C, 55·5; H, 5·2%; *M*, 324; reactive H, 0·93%]. Leucodri has specific rotatory power $[\alpha]_D$ − 15·45° (from Merck, *loc. cit.*). In aqueous solution, i neutralised baryta slowly in the cold. Titrations were carried out by the addition of exce of N/20-baryta and back-titration in the hot; the end-point was rather indefinite [Found equiv., 155. Calc. for $C_{15}H_{16}O_8$ (two lactone groups): equiv., 162].

iso*Propylidene Leucodrin.*—Leucodrin (2 g.) was dissolved in dry acetone (150 c.c.), and di hydrogen chloride passed in until its concentration was 0·5%. The mixture was left at roo temperature overnight, the mineral acid then neutralised with lead carbonate, and the filter solution evaporated; the residue crystallised on scratching. It was dissolved in alcohol, ai water added in suitable amount; on freezing, iso*propylidene leucodrin* separated in colourle prisms, m. p. 229·5—231·5° [Found: C, 58·9; H, 5·5; reactive H (Zerewitinow estimati in pyridine), 0·60. $C_{18}H_{20}O_8$ (two reactive hydrogens) requires C, 59·3; H, 5·5; reacti H, 0·55%].

*Diacetyl* iso*propylidene leucodrin* separated as an oil when water was added to a soluti of *iso*propylidene leucodrin (2 g.) in pyridine (3 g.) and acetic anhydride (1·5 g.) which had be kept overnight; it crystallised in contact with ethyl alcohol, and separated from this solv in elongated prisms, m. p. 168—169° (Found: C, 58·6; H, 5·3. $C_{22}H_{24}O_{10}$ requires C, 58 H, 5·4%).

*The Action of Ammonia, Ethylamine, and Benzylamine on Leucodrin.*—Leucodrin (1 g.) was added to a dry saturated solution of ammonia in methyl alcohol (10 c.c.); after 24 hours the corresponding *dihydroxydiamide* crystallised. Recrystallised from methyl alcohol, it formed long matted needles, m. p. 175—176° with evolution of gas. Freed from solvent, the material was very hygroscopic (Found: C, 50·5; H, 6·5; N, 7·8. $C_{15}H_{22}O_8N_2$ requires C, 50·3; H, 6·2; N, 7·8%).

In a similar manner ethylamine and leucodrin yielded the corresponding *dihydroxybisethylamide*, which crystallised from water in prisms, m. p. 184—185° with evolution of gas (Found: C, 55·5; H, 7·7; N, 7·0. $C_{19}H_{30}O_8N_2$ requires C, 55·2; H, 7·3; N, 6·8%).

The *dihydroxybisbenzylamide* was recrystallised from aqueous alcohol. It effervesced and melted when placed in a bath above 130°, solidified, and remelted at 212°. When, however, the substance was placed in a bath below 130°, no visible effervescence occurred, the substance remaining unmolten till 212° (Found for substance dried in a vacuum at 80°: C, 65·0; H, 6·5; N, 4·9. $C_{29}H_{34}O_8N_2$ requires C, 64·7; H, 6·4; N, 5·2%).

*Acetylation.*—Leucodrin was heated with acetic anhydride alone for 15 hours, or in the presence of anhydrous sodium acetate or pyridine. The product, which could be hydrolysed back to leucodrin, crystallised from acetic acid in prisms, m. p. 191—192° [Found: C, 56·0, 55·9; H, 5·1, 5·0; $CH_3$·CO, 36·0. $C_{15}H_{12}O_8(CO{\cdot}CH_3)_4$ requires C, 56·1; H, 4·9; $CH_3$·CO, 35·0%]. It appears to be a *tetra-acetyl leucodrin.*

*Leucodrin Methyl Ether.*—Leucodrin (10 g.) was dissolved in dry methyl alcohol (60 c.c.) and treated with an ethereal solution of diazomethane (from nitrosomethylurea, 15 g.). After 12 hours any excess of diazomethane was destroyed and the solvents were evaporated. The viscous residue crystallised in only a few experiments. In difficult cases, the product could sometimes be obtained crystalline by boiling the oily product in alkaline solntion for a few minutes, acidifying the solution, and evaporating it. Radiating clusters of crystals then separated; these melted indefinitely above 90°, the melt solidifying and remelting at 174—175°. This behaviour was due to water of crystallisation, which was gradually removed above 100° [Found: C, 54·3, 54·0; H, 5·7, 6·0; $H_2O$ (lost at 100°), 5·1; reactive H, 1·01; OMe, 8·6. $C_{16}H_{18}O_8,H_2O$ (four reactive hydrogens) requires C, 53·9; H, 5·6; $H_2O$, 5·4; reactive H, 1·12; OMe, 8·7%]. On oxidation with potassium permanganate solution, this *methyl* ether yielded anisic acid, thus proving that the methyl group had been introduced on a phenolic hydroxyl group. It was insoluble in sodium bicarbonate solution, but soluble in caustic alkali [Found: equiv. by back-titration in the hot, 170. $C_{15}H_{18}O_8$ (two lactone groups) requires equiv., 169]. Attempts to prepare an acetyl derivative in the usual way led to oily viscous products which could not be purified. On potash fusion, it yielded, not anisic acid as expected, but a mixture of *p*-hydroxybenzoic acid and β-*p*-hydroxyphenylpropionic acid.

iso*Propylidene-leucodrin Methyl Ether.*—Leucodrin methyl ether was treated with acetone and hydrogen chloride as in the preparation described for *iso*propylidene leucodrin. The viscous product was taken up in acetone, and water added; on cooling in ice, iso*propylidene-leucodrin methyl ether* crystallised slowly in prisms, m. p. 161·5—162·5° [Found: C, 60·9; H, 5·7; reactive H, 0·3. $C_{19}H_{22}O_8$ (one reactive H) requires C, 60·4; H, 5·8; reactive H, 0·26%]. In later experiments, this substance was obtained in better yields by the action of diazomethane on *iso*propylidene leucodrin.

*Acetyl-*iso*propylidene-leucodrin Methyl Ether.*—*iso*Propylidene-leucodrin methyl ether (1 g.) was treated with a mixture of pyridine (1·5 c.c.) and acetic anhydride (0·7 c.c.) in the cold. After 12 hours water was added, and the *product* recrystallised from ethyl alcohol. It separated in prisms of hexagonal outline, m. p. 160·5—161·5° (Found: C, 60·0; H, 6·0. $C_{21}H_{24}O_9$ requires C, 60·0; H, 5·7%).

*Bromoleucodrin methyl ether*, obtained from leucodrin methyl ether by the action of bromine in methyl-alcoholic medinm, crystallised from aqueous alcohol in colourless prisms of rectangular outline, m. p. 243—244° after sintering at 238°. It was soluble in caustic alkali but insoluble in sodium bicarbonate solution [Found: C, 46·3; H, 4·1; Br, 18·3; equiv., by back-titration in the hot, 205. $C_{16}H_{17}O_8Br$ (two lactone groups) requires C, 46·0; H, 4·1; Br, 19·1%; equiv., 208·5].

iso*Propylidene-bromoleucodrin methyl ether*, recrystallised from methyl alcohol, formed white plates, m. p. 108—110° (Found: C, 49·6; H, 4·6; Br, 17·3. $C_{19}H_{21}O_8Br$ requires C, 49·9; H, 4·6; Br, 17·5%).

*Fusion of Leucodrin with Alkalis.*—Leucodrin (3 g.) was mixed with sodium hydroxide (9 g.) and potassium hydroxide (6 g.), water added, and the mixture stirred at 220° for 25 minutes. The cooled melt was dissolved in as little water as possible, the solution acidified

with sulphuric acid and extracted with ether, the extracts dried, and the ether evaporated. The solid residue smelt strongly of acetic acid and of phenol. By a long series of fractional crystallisations from water it was separated into *p*-hydroxybenzoic acid and β-*p*-hydroxyphenylpropionic acid, m. p. 128·5—129·5° (Found: C, 65·1; H, 6·1. Calc. for $C_9H_{10}O_3$: C, 65·1; H, 6·0%). The latter was identified by a mixed m. p. test with an authentic specimen prepared from phloridzin (Cremer and Seuffert, *Ber.*, 1912, **45**, 2566). Since β-*p*-hydroxyphenylpropionic acid yields phenol, *p*-hydroxybenzoic acid, and acetic acid on fusion with potash (Barth, *Annalen*, 1869, **152**, 96; Barth and Schreder, *Ber.*, 1879, **12**, 1259), the presence of traces of phenol and of acetic acid in the crude product was explained.

*Dibromoleucodrin.*—Leucodrin (6 g.) in methyl alcohol (50 c.c.) was treated in the cold with bromine (6·5 g.) in methyl alcohol (50 c.c.). The mixture became warm, and the methyl alcohol and the slight excess of bromine were then distilled off. The residue crystallised from methyl alcohol in colourless prisms, m. p. 254—255° [Found: C, 37·0, 37·5; H, 3·3, 3·3; Br, 33·2, 33·3; reactive H (Zerewitinow estimation in pyridine), 0·66, 0·67. $C_{15}H_{14}O_8Br_2$ (three reactive hydrogens) requires C, 37·3; H, 3·0; Br, 33·2; reactive H, 0·64%]. *Dibromoleucodrin* was soluble in sodium bicarbonate solution. For titration experiments, it was dissolved in alcohol and titrated with N/20-baryta, back-titration in the hot being used: the titre was three times that required to bring the solutions to neutrality in the cold [Found: equiv., by back-titration, 160. $C_{15}H_{14}O_8Br_2$ (one acidic and two lactone groups) requires equiv., 161].

In quantitative brominations of leucodrin, this substance was dissolved in water, an excess of N/10-potassium bromide–bromate mixture added, and the whole acidified. After 15 minutes the excess of bromine was estimated iodometrically [Found: *M* (assuming dibromination), 323. Calc. for $C_{15}H_{18}O_8$: *M*, 324].

*Tetra-acetyl Dibromoleucodrin.*—On acetylation with acetic anhydride dibromoleucodrin yielded a solid substance, which crystallised from dilute acetic acid in colourless prisms, m. p. 195—196° [Found: C, 42·4; H, 3·4; Br, 24·5; CO·CH₃, 25·4. $C_{15}H_{10}O_8(CO{\cdot}CH_3)_4$ requires C, 42·4; H, 3·5; Br, 24·5; $CO{\cdot}CH_3$, 25·2%], insoluble in sodium bicarbonate solution.

*Tetrapropionyl dibromoleucodrin*, prepared with propionic anhydride, crystallised from dilute propionic acid or from alcohol in matted needles, m. p. 106—108° [Found: C, 46·2; H, 4·4. $C_{15}H_{10}O_8Br_2(CO{\cdot}CH_2{\cdot}CH_3)_4$ requires C, 45·9; H, 4·3%].

*Dichloroleucodrin.*—This was formed by the repeated evaporation of a leucodrin solution in the presence of concentrated hydrochloric acid and hydrogen peroxide. It crystallised from water in colourless prisms, m. p. 236·5—239°, and in all its properties resembled the corresponding dibromoleucodrin [Found: C, 46·4, 46·0; H, 3·7, 3·8; Cl, 17·4; equiv., by back titration, 129. $C_{15}H_{14}O_8Cl_2$ (one acidic and two lactone groups) requires C, 45·8; H, 3·6; Cl, 18·0%; equiv., 131].

*Tetra-acetyl dichloroleucodrin* crystallised from slightly diluted acetic acid in colourless prisms, m. p. 171—172°. Like the corresponding dibromo-compound, it was insoluble in sodium bicarbonate solution, and could not be titrated with alkali in the cold [Found: C, 49·6; H, 4·3; Cl, 12·8; $CO{\cdot}CH_3$, 30·5. $C_{15}H_{10}O_8Cl_2(CO{\cdot}CH_3)_4$ requires C, 49·1; H, 4·1; Cl, 12·6; $CO{\cdot}CH_3$, 30·1%].

*The Action of Nitric Acid on Leucodrin.*—To leucodrin (1 g.), moistened with water, was added a mixture of nitric acid (4 c.c.) and water (6 c.c.); the whole became warm and orange-red. The crystals obtained after heating on the water-bath for a few minutes were collected, washed with water, and recrystallised from this solvent. The new substance separated in long, flat slightly yellow prisms. It dissolved readily in sodium bicarbonate solution and in alkalis tc give deep orange solutions. The crystals decomposed slowly above 240°, and melted to a darl liquid at 251° [Found: C, 43·9, 43·7; H, 3·6, 3·7; N, 7·0, 7·0. $C_{15}H_{14}O_8(NO_2)_2$ requires C 43·5; H, 3·4; N, 6·8%]. It appears as if a *dinitroleucodrin* had been formed. With highe concentrations of nitric acid, oily products resulted.

The author thanks Prof. R. H. Compton of the National Botanic Gardens, Kirstenboscl for his assistance in collecting some of the materials required for this investigation.

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## 58. *Mechanism of Polymerisation. Part III. Experiments relating to the Constitution of the Solid Dimeride and the Liquid Trimeride of βγ-Dimethylbutadiene.*

By Ernest Harold Farmer and Robert C. Pitkethly.

The solid camphor-like dimeride formed together with various liquid dimerides by the action of the Bertram–Walbaum reagent on βγ-dimethylbutadiene appears from its behaviour towards additive reagents and on oxidation to be a mono-olefinic dicyclic hydrocarbon containing a reactive methylene group. Its behaviour with chromic acid and ozone is highly characteristic and is reminiscent of that of α-fenchene and of camphene with the same reagents. Consideration of the ways in which methylene-bicyclanes could be formed *directly* and simply from the monomeride suggest that the dimeride is either a trimethylmethylene*bicyclo*[2 : 2 : 2]octane or a tetramethylmethylene*bicyclo*[1 : 2 : 2]heptane.

The trimeric material from βγ-dimethylbutadiene is heterogeneous in constitution, but a fraction (30%) of constant refractive index can be isolated. This, on the basis of its additive behaviour, its behaviour on oxidation, and the fact that it gives a naphthalenic hydrocarbon on dehydrogenation, is thought to consist substantially of an alkenylhydronaphthalene, which may well be pentamethyl*iso*propenyloctahydronaphthalene.

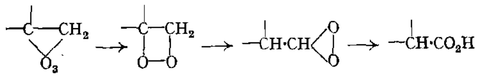
*The Solid Dimeride.*

βγ-Dimethylbutadiene, when polymerised in an acid medium, gives a liquid monocyclic dimeride, a solid camphor-like dimeride, $C_{12}H_{20}$ (m. p. 66°), and probably two liquid dicyclic dimerides (this vol., p. 11). Although the solid dimeride can be made to react with 2 mols. of bromine when treated with pyridine perbromide, it is definitely mono-olefinic as determined by hydrogenation at atmospheric pressure and by reaction with perbenzoic acid; moreover, its dihydride is unreactive towards bromine. This behaviour, taken together with the way in which the dimeride reacts with oxidising agents (below), leaves little doubt that it is dicyclic in character.

Oxidation of the dimeride with chromic acid gives at once a crystalline monobasic acid, $C_{12}H_{20}O_2$, the reaction involving mere incorporation of oxygen atoms in the molecule and simulating that which occurs with two well-known methylene-dicyclanes, α-fenchene and camphene :

$$C_8H_{14}{>}C{:}CH_2 \xrightarrow{2O} C_8H_{14}{>}CH{\cdot}CO_2H \quad (I.)$$

Treibs and Schmidt (*Ber.*, 1928, **61**, 459) showed that α-fenchene passes on treatment with chromic acid into a mixture of fenchenylanic acid (I) and fenchenylanaldehyde, $C_8H_{14}{>}CH{\cdot}CHO$ (II) (together with some α-fenchocamphorone, $C_8H_{14}{>}CO$); and Komppa and Roschier (*Ann. Acad. Sci. Fennicæ*, 1917, *A*, **10**, xviii, 1; *Annalen*, 1929, **470**, 129) showed that it gives on ozonolysis a mixture of this same acid and ketone. The latter authors have suggested that the acid is formed from the ozonide by the unusual rearrangement :



In the oxidation of α-fenchene by chromic acid, the aldehyde (II) seems to be the primary product, and the acid (I) to be formed from it by secondary reaction. Now it has been found in the case of a third well-known methylene-dicyclane, β-pinene, that conversion of the methylene-hydrocarbon into the aldehyde can be conducted in two distinct stages, *viz.*, by transformation first into the corresponding glycol with permanganate, and thence into the aldehyde (with some pinol as by-product) by the action of hot dilute acids :

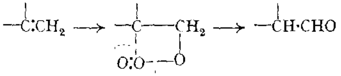
$$C_8H_{14}{>}C{:}CH_2 \longrightarrow C_8H_{14}{>}C(OH){\cdot}CH_2{\cdot}OH \longrightarrow C_8H_{14}{>}CH{\cdot}CHO$$

Another example of this two-stage oxidation is afforded by the conversion of β-phellandrene into phellandral *under similar conditions.* Hence we suggest that the course of oxidation *in* acid media of *all* the above-named terpenic methylene compounds is the following :

$$>C{:}CH_2 \xrightarrow[(H_2O)]{O} >C(OH){\cdot}CH_2{\cdot}OH \xrightarrow{-H_2O} >C{:}CH{\cdot}OH \longrightarrow >CH{\cdot}CHO \longrightarrow >CH{\cdot}CO_2H$$

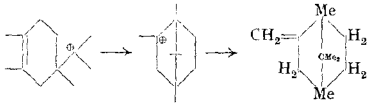
and that the aldehyde $C_{12}H_{20}O$ in the present work is produced from the solid dimeride of dimethylbutadiene in exactly this way.

If this is correct and the solid dimeride has an extracyclic methylene group, the dimeride should give on ozonolysis formaldehyde and a cyclic ketone (as do the methylene-hydrocarbons β-pinene and selinene: Brus and Peyresblauques, *Compt. rend.*, 1928, **187**, 194; Schmidt, *Z. angew. Chem.*, 1929, **42**, 126; Ruzicka and Stoll, *Helv. Chim. Acta*, 1922, **5**, 926), provided reaction follows a normal course. In practice, however, we have been able to obtain only a very small yield of formaldehyde from the ozonolysis product, but on the other hand have obtained approximately a 50% yield of a monocarbonyl derivative, $C_{12}H_{20}O$ (not a dicarbonyl derivative as would be expected from a dicyclene in contradistinction to a methylene-dicyclane); in other words, ozonolysis brings about oxidation without loss of any carbon atoms of the molecule, and this can only mean that *the carbonyl derivative $C_{12}H_{20}O$ is the aldehyde corresponding to the saturated acid* ($C_{12}H_{20}O_2$) produced by chromic acid oxidation of the dimeride (above), and is formed by some such mechanism as :



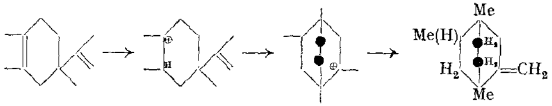

In the formation of a methylene-dicyclane by dimerisation of an open-chain diene the first step is with little doubt the production of an open-chain dimeric structure, which subsequently undergoes two stages of cyclisation. Now it is possible that the monocyclic dimeric kation (III), which we regard as the probable precursor of the ordinary liquid

(III.)




(IV.)

(V.)




(VI.)

dimeride (V) (see this vol., p. 11) * passes in part by transannular addition directly int the methylene-dicyclane (IV); on the other hand, the solid dicyclic dimeride may wel be formed directly from (V) and may thus have the formula (VI). Of the formulæ (IV and (VI),† we consider (VI) probably to represent the solid dimeride, since existin

* Free-radical structures equivalent in their essential characteristics to the primarily formed, open chain dimeric kation and to the derived monocyclic kation (III) could be postulated as intermediate in the case of thermal polymerisations (compare Harkness, Kistiakowsky, and Mears, *J. Chem. Physic.* 1937, **5**, 69†), but are hardly likely to appear in acid-catalysed polymerisations in solution. It ma be remarked here that the experimental evidence advanced by Harkness and his collaborators (*loc. cit* as indicating the non-formation of any proportion of cyclic dimeride during the thermal dimerisatic of gaseous butadiene is hardly more convincing than Vaughan's earlier evidence to the contrary ( *Amer. Chem. Soc.*, 1932, **54**, 3863; 1933, **55**, 4109).

† Other structures (" meta "-bridged) could be formulated, but are not considered likely to 1 produced.

evidence indicates that the ease of formation and freedom from strain of *bicyclo*[1 : 2 : 2]-heptanes is inferior to that of *bicyclo*[2 : 2 : 2]octanes; but it is to be borne in mind that the conversion at will of the ordinary dimeride (V) into the solid dimeride has not yet been effected.

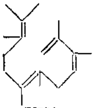
### *The Liquid Trimeride.*

The trimeric fraction, when separated by distillation from dimeric, tetrameric, and higher polymeric material, was evidently not homogeneous in constitution, since its sub-fractions differed considerably in physical properties. A portion of the trimeric fraction of nearly constant refractive index was separated by systematic fractionation and this was used for investigation. The analytical figures, molecular weight (in benzene), and molecular refractivity of this portion agreed with the values required for a diolefinic *dicyclic* trimeride, $C_{18}H_{30}$.

Although only one double bond in the trimeric molecule could be saturated by catalytic hydrogenation at atmospheric pressure and room temperature, yet the trimeride absorbed two molecules of bromine, and its dihydride one molecule of bromine. With permanganate the trimeride underwent rapid oxidation at room temperature, but its dihydride was attacked only very slowly. On ozonolysis the trimeride gave formaldehyde (0·2 mol.) together with a ketonic oil, and other materials which have not been investigated. The formation of the formaldehyde points to the presence of a methylene group in at least one-fifth of the material ozonised.

On dehydrogenation with selenium the trimeride gave a mixture of hydrocarbons, from which could be isolated *via* its *picrate* a crystalline aromatic hydrocarbon, $C_{17}H_{22}$, m. p. 111°. With this proportion of carbon to hydrogen the hydrocarbon can hardly be other than a substituted naphthalene ($C_{10}H_8 + 7CH_2$) and, since it is impossible to construct an anthracene or phenanthrene nucleus by union of three molecules of βγ-dimethylbutadiene, the mere fact of the formation of a picrate lends strong support to this conclusion.

It is uncertain whether the dicyclic trimeride which gives the naphthalenic hydrocarbon on dehydrogenation is to be regarded as derived by two stages of cyclisation from a preformed open-chain trimeric structure (hydrocarbon or kation) or by the addition of dimethylbutadiene to the ordinary dimeride (V) or to a kationic form thereof. If the former mechanism is correct, the open-chain structure would have the structure (VII) and would yield a dicyclic derivative having the skeleton (IX) [compare the conversion of farnesene (VIII) into dicyclic *iso*cadiuene; Henderson and Robertson, J., 1926, 2811]; but if the latter is correct, the dicyclic derivative might have any one of the skeletons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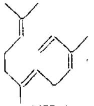
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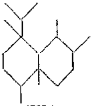
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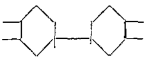
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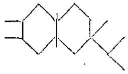
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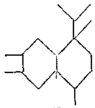
(XII.)

(IX)—(XII). Substances having the skeletons (X) and (XI) would only arise if dimethylbutadiene were to add to one or to the other bond of the dimeride in the way (Diels–Alder type of reaction) that *cyclo*pentadiene is reputed to add to di*cyclo*pentadiene (Alder, Stein, and Finzenhagen, *Annalen*, 1931, **485**, 223; Alder and Stein, *ibid.*, 1932, **496**, 197, 204). This we hold to be extremely unlikely, since on the one hand (XI) would be the product of addition occurring at the endocyclic double bond of the dimeride, which is the less

reactive bond of the two, and on the other hand the formula (X) clearly cannot apply because a substance having this skeleton would give a derivative of diphenyl on dehydrogenation and hence would not yield a picrate.

In dehydrogenation reactions with selenium the methyl groups of the quaternary carbon groupings >CMeR and ⋝CMe are usually eliminated (*e.g.*, in selinene, ionene, the sterols, and various synthetic compounds). The structure (XI) has three such groupings, and (IX) and (XII) have two; but as only one methyl group is lost in practice, it follows that one or two methyl groups (presumably situated in bridge-head positions) must escape elimination by migration. Recent work by Linstead and his collaborators on 9-methyloctalin and 4 : 9-dimethyloctalin (J., 1937, 1146) has shown that a methyl group can migrate from a bridge-head position to an adjacent carbon atom when sulphur is the dehydrogenating agent. We suggest, therefore, that the aromatic hydrocarbon isolated from the trimeride is a *tetramethyl*iso*propylnaphthalene* derived from a trimeride having the carbon skeleton (IX), (XI) or (XII), but most likely from one having the skeleton (IX) or (XII). Up to the present it has not been possible to distinguish between these formulæ.

Without doubt other hydrocarbons are present in the trimeric fraction and it is probable that the tetrameric and higher fractions also represent mixtures of isomeric hydrocarbons. It is hoped later to resume the study of the trimeric and the tetrameric products of acid-catalysed polymerisation.

## EXPERIMENTAL.

*The Solid Dimeride.*—This was obtained in 1·6% yield by treatment of βγ-dimethylbutadiene with a Bertram–Walbaum reagent containing 1% of concentrated sulphuric acid (this vol., p. 11). It absorbed only 1 mol. of hydrogen (Found : 0·986 mol.) when exhaustively hydrogenated (Adams's catalyst) in acetic acid; furthermore, when it was treated at room temperature in pure chloroform with perbenzoic acid, and the excess of reagent determined after periods ranging from 5 minutes to 24 hours by means of potassium iodide and standard thiosulphate solution, it was found that the unsaturation–time relationship could be represented by a smooth curve in which the observed unsaturation increased asymptotically to a maximum of 1·0 double bond. When, however, the dimeride was treated with bromine under Rosenmund and Kuhnhenn's conditions (*Z. Unters. Nahr. Genuss.*, 1923, **46**, 154), 2 mols. of halogen were absorbed (Found : 2·02, 2·015), the second molecule apparently by substitution.

When the solid dimeride was melted with an equimolecular quantity of maleic anhydride, a yellow coloration developed, and was especially marked in the anhydride layer. No combination, however, took place, nor could any combination be effected in benzene solution.

*Oxidation.* The hydrocarbon (0·5 g.), dissolved in glacial acetic acid (15 c.c.), was treatec very slowly (2 hours) at 80° with chromic acid (1·65 g.) dissolved in 50% acetic acid (10 c.c.) The product was heated on a steam-bath for 2 hours and then kept overnight at roon temperature; afterwards it was diluted with water (150 c.c.) and the flocculent precipitat which separated was filtered off, dried, and extracted with light petroleum. The solid (0·1 g. recovered from the solvent was an acid, which, after reprecipitation from solution in sodiun carbonate solution and crystallisation from light petroleum, formed colourless leaflets, m. p 119°. This substance, for reasons already given (p. 288), is considered probably to b 1 : 2 : 4-*trimethyl*-1 : 4-endo*ethylene*cyclo*hexane*-5-*carboxylic acid* [Found : C, 73·7; H, 9·9 *M* (monobasic), 193·6. $C_{12}H_{20}O_2$ requires : C, 73·4; H, 10·25%; *M*, 196·3]. From th aqueous oxidation liquor a small amount of intractably gummy material was recovered.

*Ozonolysis.* The solid dimeride (0·5 g.), dissolved in pure *alcohol-free* chloroform (90 c.c. was ozonised at 0°. The solution of the ozonide was refluxed for 1½ hours with water, an the chloroform layer then separated and washed with water. The aqueous solution an washings, when tested with 2 : 4-dinitrophenylhydrazine, gave only a trace of formaldehyd 2 : 4-dinitrophenylhydrazone (m. p. and mixed m. p. 162°).

The chloroform layer contained no acidic material: it was accordingly dried an evaporated, yielding a rather intractable, pasty mass of camphor-like odour. This materi coloured Schiff's reagent, but was not oxidised at room temperature by permanganate : it ga a *semicarbazone*, probably that of 5-*aldehydo*-1 : 2 : 4-*trimethyl*-1 : 4-endo*ethylene*cyclo*hexa* which after several recrystallisations from methyl alcohol melted at 224° (Found : C, 65· H, 9·7; N, 17·9. $C_{13}H_{23}ON_3$ requires C, 65·85; H, 9·7; N, 17·7%).

*The Trimeric Fraction.*—For the production of trimeric βγ-dimethylbutadiene in quantity the polymerisation of the hydrocarbon was conducted preferably with a reagent containing 1% of sulphuric acid. The polymeric material remaining after the dimeride fraction had been distilled (this vol., p. 16) gave on continued distillation a fairly definite, trimeric fraction (b. p. 120°/20 mm.—120°/1 mm.); the boiling point then rose continuously to 180°/0·5 mm. and a large residue remained. Distillation of the residue could be continued in a molecular still until only a black viscous resin (solid when cold) remained.

The crude trimeric fraction was refractionated slowly (controlled reflux ratio) at 0·5 mm. pressure under a 45 cm. vacuum-jacketed column, packed with a nichrome wire spiral, the progress of distillation being followed by determining the refractive index of each fraction and plotting these values against the total proportion (%) of material distilled at the end of each fraction. Five fractions were at first collected and these were subdivided in subsequent series of distillations, the individual fractions obtained being combined or segregated according to the correspondence or otherwise of their refractive indices. At the sixth series of distillations nearly 30% of the material distilled had a practically constant refractive index. This portion had $n_D^{24.5°}$ 1·49345, $d_{4°}^{24.5°}$ 0·8952, $[R_L]_D$ 80·04 (calc. for $C_{18}H_{30}|\overline{_2}$, 79·99), *M* (in benzene) 252, 250 (calc. 246·2), and was used in the following experiments.

When brominated by the method of Rosenmund and Kuhnhenn, the trimeride took up 2 mols. of bromine (Found: 1·99, 1·99), but when hydrogenated at room temperature (Adams's catalyst) in either alcohol or acetic acid, it took up only 1 mol. of hydrogen (Found: 1·01, 1·01). Towards permanganate the trimeride was very unstable, and the aqueous oxidation product after neutralisation readily reduced warm silver nitrate solution.

The *dihydride* obtained by hydrogenation of 5 g. of trimeride distilled at 140—149°/12 mm., but on redistillation a third of the material distilled at 139·5—141·5°. This had $n_D^{17°}$ 1·4878, $d_{0°}^{17°}$ 0·88815, $[R_L]_D$ 80·57 (calc. for $C_{18}H_{32}|\overline{_1}$, 80·46) (Found: C, 86·9; H, 12·85. $C_{18}H_{32}$ requires C, 87·0; H, 13·0%). The dihydride absorbed 0·98 mol. of bromine when treated with pyridine perbromide under the conditions of Rosenmund and Kuhnhenn, but was not attacked by permanganate at room temperature.

*Ozonolysis.* The trimeride was ozonised in chloroform, and the solution refluxed with water. The aqueous solution so obtained contained formaldehyde and this was isolated in the form of its 2 : 4-dinitrophenylhydrazone, m. p. 162° (yield, 0·2 mol.). The chloroform solution yielded an oil, which was treated with the Girard reagent "T" in order to isolate the ketonic component. The latter, regenerated from combination with the reagent, was an oil which gave with semicarbazide hydrochloride a very small quantity of a solid derivative. The nature of this derivative and of the remaining ozonolysis products has not been determined.

*Dehydrogenation of the Trimeride.*—The trimeride (6 g.), when dehydrogenated at 340° ± 10° for 40 hours with selenium (10 g.), gave a dark brown, slightly fluorescent oil (5 g.), which was first distilled and then refluxed for some time with sodium in ether. The product was freed from the reagent and fractionated. Six fractions boiling between 260° and 300° were collected, and each of these was separately treated with a solution of picric acid in methyl alcohol. Five of the fractions gave some proportion of orange crystals, and these crystals when combined and recrystallised several times from methyl alcohol formed bright orange needles (0·75 g.), m. p. 156°. This was the *picrate* of a hydrocarbon $C_{17}H_{22}$ (Found: C, 60·45, 60·7; H, 5·6, 5·45. $C_{17}H_{22},C_6H_3O_7N_3$ requires C, 60·65; H, 5·5%).

When heated for 15 minutes at 100° with 10% caustic soda solution, the picrate gave an oil which solidified on cooling. This was a *hydrocarbon*, apparently (although not certainly) tetramethyl*iso*propylnaphthalene, which formed colourless needles, m. p. 111°, when twice crystallised from methyl alcohol (Found: C, 90·1; H, 9·65. $C_{17}H_{22}$ requires C, 90·26; H, 9·7%).

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Imperial College, London, S.W. 7. [Received, January 22nd, 1938.]

# 59. *Structure of the Copper Lakes of Azo-dyes.*

By H. D. K. Drew and J. K. Landquist.

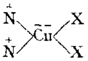
Lake formation with copper increases the stability of azo-compounds, particularly towards light, but little is known to account for the effect. Only in a few of the less complex cases have the lakes been isolated and their structures determined. The present paper describes copper lakes of *o*-hydroxy-, *o*-carboxy-, *oo'*-dihydroxy-, *o*-hydroxy-*o'*-carboxy-, and *oo'*-dicarboxy-azo-compounds of the benzene and the naphthalene series, and some examples in which one hydroxyl group is *m*- or *p*- to the azo-group; lakes of *o*-hydroxy-azo-sulphonic acids also are described, together with some simple copper salts of these acids. The structures of the lakes and their stereochemical forms are discussed, and the general principles governing the formation of the lakes are indicated. The results of the work imply that the stability of the lakes is enhanced among those which have inner co-ordination of copper with azo-nitrogen, and that such forms arise only when copper is affixed by covalent linkings to substituents (such as OH, $CO_2H$, or $NH_2$) which are in the *o*-position to the azo-groups, *m*- or *p*-hydroxyls having little or no effect; the presence of two substituents of this kind (particularly two hydroxyl groups) in the *oo'*-positions further increases the stability, the lakes assuming fused-ring forms. The inner co-ordinated copper lakes of sulphonic and carboxylic acids of the *o*-monohydroxy-azo-series are formed only when the acid groups are neutralised by further copper atoms or by other metals or groups. Copper attached to a sulphonic acid group is capable of transference to the inner co-ordinated state under certain conditions. Some of the lakes exhibit co-ordinative unsaturation when prepared by normal means, and this property has been made use of to determine their structures.

The special properties of the metallic lakes of azo-dyes containing the hydroxyl or amino-group in an *o*-position to the azo-group have led many authors to assume co-ordination of the metallic atom with one or both nitrogen atoms of the azo-group (see, for example, Werner, *Ber.*, 1908, **41**, 1062; Baudisch, *Z. angew. Chem.*, 1917, **30**, 133; Morgan and Main Smith, J., 1924, **125**, 1731; Charrier and Beretta, *Gazzetta*, 1926, **56**, 865; Crippa, *ibid.*, 1927, **57**, 20; Cremonini, *ibid.*, 1928, **58**, 372; Elkins and Hunter, J., 1935, 1598); but so varied are the structural possibilities among the copper derivatives of the azo-compounds that principles governing the formation of these lakes have not been defined in the literature, except as regards those of mono-*o*-hydroxy- and -amino-compounds. The position with respect to the stereochemistry of the lakes is still more obscure, and is complicated by the lack of general agreement as to the space structure of tervalent nitrogen and of 4-covalent copper.

Owing to the variable co-ordination number of bivalent copper and to the uncertainty as to whether the metal is to be regarded in all cases as covalently linked with or as ionised from the oxygen of hydroxyl, carboxyl, or sulphonic acid groups in the neighbourhood of the azo-group, it was not at first possible to apply the principles of Werner; but as the work progressed, a review of the data brought us to the conclusion that the stable co-ordination compounds of cupric copper are ordinarily those in which the copper atom is associated with 35 planetary electrons (*i.e.*, the atomic number of copper, together with 6 additional electrons from attached atoms), but that in the copper lakes of azo-compounds this number of electrons may fall short of 35 by one or more pairs. When this occurs, the lake will exhibit co-ordinative unsaturation and will tend to combine with one or more molecules of water, ammonia, or the like. Further, when water and the like are present in the lake the number of associated planetary electrons may in rarer instances be exceeded by one or more pairs, in which case the lake will tend to lose co-ordinating molecules until the number of electrons associated with the copper atom has reached 35. The azo-group of aromatic substances shows, so far as we could find, little or no co-ordinating power for a metal atom not already attached by some other group in an *o*-position to the azo-group, and therefore external molecules of the azo-dye are not combined in excess with the metal nor can azo-dye molecules be eliminated from the complex, as is the case, for example, with ammonia. There are then three ways in which an atom of bivalent copper can become saturated

co-ordinatively in these lakes : it may be (1) non-ionised and co-ordinated with two nitrogen or other atoms, or (2) singly ionised and co-ordinated with three atoms, or (3) doubly ionised and co-ordinated with four atoms. Our experience has been that the second of these modes is rarely found. It happens sometimes that the lakes isolated are not co-ordinatively saturated and they may be well-defined and apparently stable substances; in these cases the degree of co-ordinative unsaturation can generally be determined by noting the number of ammonia or similar molecules which the lakes are capable of attaching in stable combination.

The structures of the co-ordinatively saturated lakes can be expressed by regarding the cupric atoms as having always a double negative charge (N here represents any co-ordinating atom) :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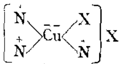
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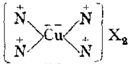
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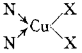
or the co-ordination bond of Sidgwick may be employed :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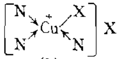
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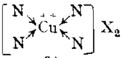
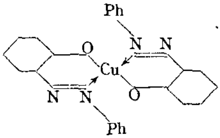

3.)

The latter system is adopted in this paper.

o-*Hydroxy-azo-compounds*.—Several authors have shown that the cupric derivatives of these substances contain one copper atom to two azo-groups. We have found that the lakes of *o*-hydroxyazobenzene, 2-hydroxy-5-methylazobenzene, 2-hydroxy-5 : 5′-dimethylazobenzene, benzeneazo-β-naphthol, and *m*-tolylazo-β-naphthol are all anhydrous. By crystallisation from pyridine, quinoline, or aniline, followed by analysis, it was shown that they are co-ordinatively saturated and do not affix further molecules of the bases. A number of structures have been attributed to this type of lake. We arrived at the general structure (as I) from the following considerations. An examination of models, from the point of view of strain, showed that a copper atom, whether planar or tetrahedral, cannot be co-ordinated with *both* nitrogen atoms of an azo-group, although such formulæ continue to appear in the literature. The copper derivatives have the characteristic properties of co-ordinated substances and are at the same time co-ordinatively saturated. They must therefore contain copper in combination with nitrogen of the azo-groups, belonging thus to type (1) above.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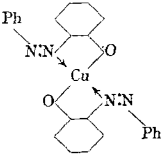
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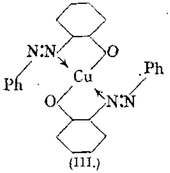
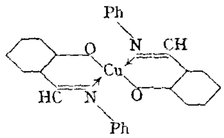
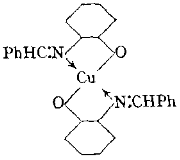

(III.)

The question whether the azo-nitrogen atoms are of *syn*- or *anti*-form then arises. Stereochemical considerations indicate that, besides the 6-ring formula (I), which has *anti*-azo-groups and copper attached to the nitrogen atom remote from hydroxyl, there are two other possible formulæ (II and III), with 5-rings, one having *syn*- and the other *anti*-azo-groups, with copper in both cases attached to the nitrogen adjacent to hydroxyl. A decision can be reached if it can be found whether the remote or the adjacent nitrogens are co-ordinated to copper. In the salicylideneimines the adjacent nitrogen atoms of the azo-compounds are replaced by carbon, which cannot co-ordinate, but Delépine (*Bull. Soc. chim.*, 1899, **21**, **944**), Barrow and Duffey (Thesis, Univ. of Lond., 1934), and others have

shown that these substances form co-ordinated copper salts of composition analogous to those of the azo-compounds; thus the copper salt of salicylideneaniline cannot have a structure analogous to (II) or (III), but must be presumed to have structure (IV). For

(IV.)



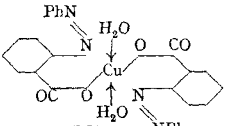


(V.)

this reason structure (I) is, by analogy, preferred for the derivatives of the azo-compounds. At the same time, the 5-ring containing copper is not excluded on principle and indeed is probable in certain cases; for example, the copper derivative of benzylidene-*o*-amino-phenol (Barrow and Duffey, *loc. cit.*) has presumably * structure (V). The 5-ring compounds, however, differ from the 6-ring in that they have comparatively high melting points and are insoluble in organic solvents.

If the quinone-hydrazone formulæ for the azo-compounds are adopted, the forms of the above structures remain unaltered, the nature of the linkings only being changed. This will be seen to hold also for certain cases mentioned later.

o-*Carboxy-azo-compounds.*—Paal (*Ber.*, 1891, **24**, 3058) obtained amorphous green precipitates from copper sulphate and ammoniacal solutions of *p*-chloro- and *p*-bromo-azobenzene-*o'*-carboxylic acids, but did not investigate them. No further work on the *o*-carboxylic acids is on record. We find that azobenzene-*o*-carboxylic acid forms the dihydrated green copper salt (VI), which is sparingly soluble in water but more soluble in benzene or chloroform.



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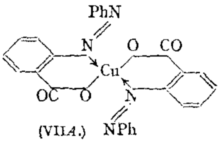
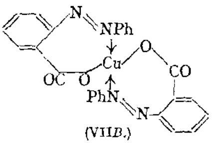


(VII*A*.)



(VII*B*.)

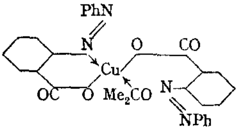
The water molecules are somewhat tenaciously held, but may be replaced by aniline or pyridine molecules. The anhydrous substance (VII), which may be obtained by boiling a benzene solution of the dihydrate to expel water and then adding petroleum, is yellow and does not crystallise from benzene or chloroform; it is soluble in many organic solvents and is rehydrated in moist air. Probably, (VII) has the co-ordinated 6-ring formula (VII*A*) where the nearer nitrogen atoms of the azo-groups, which may be either *syn* or *anti* in form are attached to the metal; but the non-planar 7-ring form (VII*B*), in which the azo-groups have the *anti*-form, would have little strain with the double bonds in the positions shown and cannot be excluded. The carboxyls are covalently linked to the metal in either case and probably the unusual co-ordination with the nearer nitrogen of the azo-groups is a weak linking which is disrupted in the presence of other co-ordinating molecules, giving, fo example, (VI) with water; an alternative, less likely from general considerations and i view of the properties of the substances, is that the covalency between copper and carbox tends to become an ionised link, the co-ordination with nitrogen being retained. It remarkable that (VI) separates from acetone as a crystalline brownish-green *monoaceto* compound which is anhydrous; this may represent the intermediate phase as shown i (VIII). An *o*-carboxyl group in azobenzene thus resembles an *o*-hydroxyl, but occasio

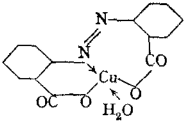
* Barrow has himself arrived at this conclusion regarding the structure of the salicylidene deri atives (private communication).

formation of a less stable link between azo-compound and metal, with the result that the copper derivative, instead of being co-ordinatively saturated, exhibits weak co-ordinating affinity, a property which may be termed pseudo-co-ordinative unsaturation.

An interesting comparison arose with azobenzene-2 : 2′-dicarboxylic acid, which formed a green copper salt, probably a dihydrate; a molecule of water was retained at 105°, the monohydrate being stable in moist air. This substance was readily decomposed by acids and by reagents which precipitate copper, and was sparingly soluble in water or in organic

(VIII.)

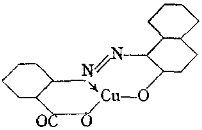




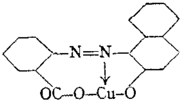
(IX.)

solvents, although it separated from pyridine as an unstable tripyridine complex. It is probable that, as in the case of the copper salt of the monocarboxylic acid, the co-ordination of the metal with nitrogen of the azo-group is feeble and is disrupted in co-ordinating solvents; it is possible also that the covalent linking between the metal and the carboxyl may become ionised in the presence of pyridine. Thus, the monohydrate may be represented by (IX); but the alternative that it is an un-co-ordinated copper salt is not entirely excluded, although the presence of the firmly bound water molecule then becomes anomalous.

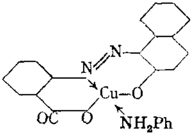
*o-Hydroxy-o′-carboxy-azo-compounds.*—Two azo-compounds of this type were studied: *o*-carboxybenzeneazo-*p*-cresol and *o*-carboxybenzeneazo-β-naphthol. These gave red-brown copper derivatives, alike in structure and exhibiting co-ordinative unsaturation; they were soluble in aniline or pyridine, forming crystalline derivatives with one molecule of these bases (as XI). The copper derivative from the second azo-compound was shown to have the simple molecular weight in pyridine and therefore the structure of these derivatives is as indicated in the 6-ring formula (X), which is not quite flat, the nuclei being slightly rotated about the bonds joining them to the azo-group; but formula (X*A*), though



(X.)



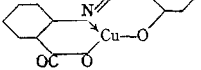
(X*A*.)

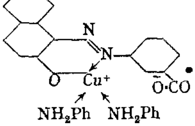


(XI.)

unlikely (see below), is also possible stereochemically. Barrow and Duffey (*loc. cit.*) obtained a green copper derivative of salicylideneanthranilic acid. If, as is probable, this substance is a true analogue of the above azo-derivatives, it must have structure (XII), similar to (X), a structure similar to (X*A*) being here impossible.

(XII.)

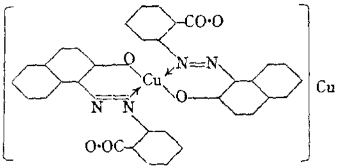




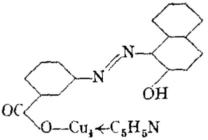
(XIII*A*.)

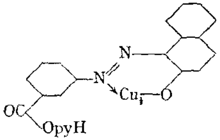
Although dimeric structures for the copper derivatives of the above azo-compounds are excluded by the molecular weight in cases where the copper is un-ionised, the structure (XIII) remains a possibility if half the copper present be considered ionised in pyridine as

solvent. In that case, however, the result would be the same if the carboxyl groups were removed to *m*- or *p*-positions, and for this reason the case of benzeneazo-β-naphthol-3′-carboxylic acid was examined. The behaviour of this azo-compound with copper salts was quite different from that of the *o*-carboxylic acids. An insoluble brown copper derivative

(XIII.) 

was prepared from cupric chloride and the sodium salt of the azo-compound, and although this was not obtained pure, it was shown to contain one copper atom to two mols. of the azo-compound; crystallised from pyridine, this salt gave a yellow-brown *dipyridine* compound of the foregoing salt, which was obtained pure in two distinct forms differing widely in colour and in their melting points (233°; 120°). The higher-melting of these forms was probably the normal salt (XIV), and the other was possibly the pyridinium salt (XV) of the co-ordinated complex. For reasons given later, in connection with the azo-

(XIV.) 

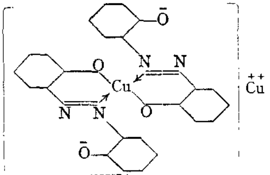
 (XV.)

sulphonic acids, two such forms might well be interchangeable under favourable conditions. There was indication of the formation, in other circumstances, of a copper salt of structure analogous to that shown in (XIII), since the substance gave rise to a tetra-aniline compound, or, alternatively, a derivative of structure (XIII*A*); but neither of these two substances was obtained pure.

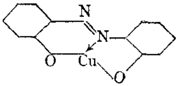
Comparison was also made with the case of benzeneazo-α-naphthol-2′-carboxylic acid. A brown copper derivative containing an atom of copper to two azo-groups was obtained in the form of a *trihydrate*; two molecules of water were tenaciously held, but were replaceable by solution in pyridine, the *dipyridine* compound being formed in red-brown crystals; aniline, however, did not combine with the copper derivative, the amorphous *anhydrous substance* separating from the hot solvent. Thus, the *p*-hydroxyl group appears to take no part in the fixation of the copper, the azo-compound behaving much like azobenzene-*o*-carboxylic acid; the dihydrated copper derivative and the dipyridine compound may therefore be regarded as similar to (VI) in structure, the anhydrous copper salt being probably like (VII*A*); in the trihydrate the loosely held third molecule of water is possibly associated with hydroxyl.

oo′-*Dihydroxy-azo-compounds.*—Although it has long been known that these substance form copper lakes, no complexes of that type have hitherto been analysed. It has bee held (see, *e.g.*, Mason, *J. Soc. Dyers and Colourists*, 1932, **48**, 293) that only one hydroxy group was in union with the metal, but the present work does not confirm this view. Bot 2 : 2′-dihydroxyazobenzene and *o*-hydroxybenzeneazo-β-naphthol gave crystalline bronze copper derivatives containing one atom of copper to one azo-group, soluble in pyridine an other organic bases to intensely purple solutions. The lakes are co-ordinatively unsaturate since they yield crystalline *monopyridine* and *monoquinoline* compounds when crystallise from these bases, although they do not combine with aniline; the combined bases a firmly held. The molecular weight of the copper lake from *o*-hydroxybenzeneazo-

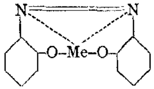
naphthol is normal in pyridine and therefore only two formulæ (XVI and XVII) are available for this type of lake. The former may be rejected for a number of reasons, *e. g.*, (a) the ionised copper atom, besides being unstably held by phenolic groups, would become



(XVI.)



(XVII.)

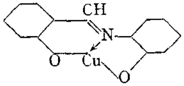


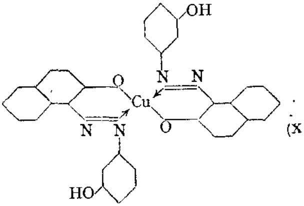
(XVIII.)

co-ordinated with four molecules of pyridine or quinoline (*i.e.*, two molecules of these bases would be present per atom of copper, instead of one as actually found), and moreover (b) it should be replaceable by sodium or other ions, whereas attempts to do this lead to a mixture of sodium and copper salts, and (c) the position of the second hydroxyl group should not be material, whereas, as will be seen later, this is not the case. The lakes, therefore, have the monomeric structure (as XVII) in which only one nitrogen of the azo-group is co-ordinated, the metal being associated in a 5- and in a 6-ring. This structure is seen from models to be very little strained, the molecule being nearly flat. The azo-group is necessarily of the *anti*-form. The degree of co-ordinative unsaturation, the high stability, and the general properties of the lakes strongly support this structure. A formula (XVIII) was proposed by Boutin (Thesis, Univ. of Lyons, 1933; see Kopp, *Bull. Soc. Ind. Rouen*, 1935, **63**, 120) for lakes of this type, but, as already pointed out, the co-ordination of a metal with both azo-nitrogens is impossible on stereochemical grounds; again, snch a structure would be co-ordinatively saturated.

The pale green *copper* salt of salicylidene-*o*-aminophenol (XIX), in which there is only one nitrogen atom, was prepared; in confirmation of the proposed structure, it was found to possess properties similar to those of the copper lakes of the above azo-compounds. On the other hand, the copper salt of disalicylidene-*o*-phenylenediamine (XX) should be saturated co-ordinatively, a point on which no data are available.

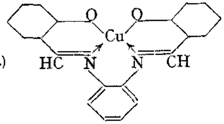
(XIX.)





(XXI.)

(XX.)



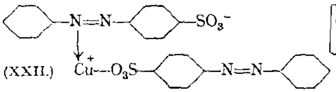
With the *oo*'-dihydroxy-azo-compounds may be compared the similar azo-compounds which have one of the hydroxyls in the *o*-position to the azo-group and the other removed to the *m*- or *p*-position in the second aromatic ring. Crippa (*Gazzetta*, 1928, **58**, 716) found that *p*-hydroxybenzeneazo-β-naphthol gives metallic lakes in which only the *o*-hydroxyl is involved, and it has now been found that *m*-hydroxybenzeneazo-β-naphthol behaves in a similar way, the copper derivative (XXI) containing two azo-groups to one copper atom. The behaviour of these azo-compounds is thus quite different from that of the *oo*'-dihydroxy-azo-compounds.

*Azo-sulphonic Acids.*—The sulphonic acid derivatives are among the most interesting

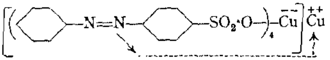
forms of the azo-compounds, on account of their dyeing properties. Because of the great variety of forms shown by the azo-sulphonic acids and the numerous structural possibilities among their metallic derivatives, the study of these substances presents a complicated problem. So far, only a few outstanding types have been examined.

(1) Azobenzene-4-sulphonic acid formed a yellow copper salt, $(C_{12}H_9O_3N_2S)_2Cu,5H_2O$, an aqueous solution of which reacted only very slowly with hydrogen sulphide or with potassium ferrocyanide and did not react with potassium iodide in the cold; with potassium iodide in the hot, or with sodium sulphide, or with pyridine and potassium thiocyanate, it gave the reactions of an ionised copper salt. In contrast, solutions of cupric benzene-sulphonate gave immediate precipitation with all the above reagents. We were unable to co-ordinate the latter salt with azobenzene. It seems probable that some kind of complex formation, accompanied by feeble co-ordination, occurs in cupric azobenzene-4-sulphonate. The ionic reactions of copper were similarly hindered in the analogous copper salts of several *o*-hydroxy-azo-compounds containing sulphonic acid groups in a *m*-, *p*-, or *peri*-position to the azo-group (see experimental section), although in each case the copper was associated with the sulphonic acid groups and not with hydroxyl.

This behaviour suggests that the cupric atoms of these salts of the sulphonic acids are in some way associated, though not strongly, with the azo-groups of the anions. This could be represented by a half ionised, half covalent structure (XXII), or by a dimeric structure (XXIII), analogous to that of $[Cu\ en_2]Cu(SO_4)_2$ and shown to be feasible from a



(XXII.)



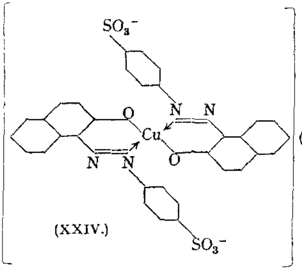
(XXIII.)

stereochemical standpoint, in which one copper atom forms part of a complex anion and the other is a cation co-ordinated with four azo-nitrogen atoms. Neither of these formulæ seems probable, and for the present it appears best to assume that in solution the cupric ions are feebly co-ordinated with azo-nitrogen atoms of the anions. In the crystalline state this union with the azo-groups is probably disrupted, being replaced by co-ordination with water or with bases. Evidence on this point is perhaps to be found in the number of molecules of water or pyridine, or both, which are associated with the crystalline salts prepared under various conditions; for example, cupric benzeneazo-β-naphthol-4-sulphonate forms a heptahydrate, a dipyridino-pentahydrate, and a tetrapyridino-trihydrate, in each of which the copper atom may be regarded as an ion associated with four water and (or) pyridine molecules, three more water molecules being associated with the sulpho-groups.

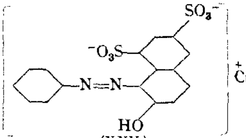
(2) o-*Hydroxy-azo-monosulphonic acids.* Of these the following were shown to form cupric salts at the sulphonic acid groups, the hydroxyls remaining free: 2-hydroxy-5-methylazobenzene-3′- and 4′-sulphonic acids, benzeneazo-β-naphthol-4′-sulphonic acid, 2-hydroxy-α-azonaphthalene-4′-sulphonic acid, and benzeneazo-β-naphthol-8-sulphonic acid. These salts, which are orange to red, are strongly hydrated and somewhat readily soluble in water.

These simple copper salts undergo a remarkable change in the presence of alkali or of certain metallic salts (*e.g.*, acetates), becoming converted into brownish-red complexes in which the copper atoms have the inner type of co-ordination, *i.e.*, are associated with the oxygens of the hydroxyl groups and with azo-nitrogen atoms instead of with the sulph groups. For example, when a solution of the simple copper salt of benzeneazo-β-naphtho 4′-sulphonic acid is treated with sodium acetate or sodium bicarbonate, it gives the amorpho complex (XXIV, R = Na), which is soluble in water with a deep brown colour; wi ammonium acetate, a similar but crystalline complex ($R = NH_4$) is produced; and wi copper acetate, a purplish-brown complex ($R_2 = Cu$), very sparingly soluble in water b somewhat soluble in pyridine or aniline. Aqueous pyridine likewise effects the transfor ation of the simple into this complex copper salt, which is obtained in the form of dipyridino-pentahydrate; a molecular proportion of the azo-compound is set free a

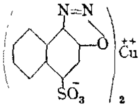
appears as the pyridinium salt. Similar inner-complex copper derivatives were obtained from 2-hydroxy-5-methylazobenzene-3′- and 4′-sulphonic acids, 2-hydroxy-α-azonaphthalene-4′-sulphonic acid, and benzeneazo-β-naphthol-8-sulphonic acid. The change seems therefore to be a general phenomenon in the *o*-hydroxy-azo-sulphonic acid series. The inner-complex copper salts are very readily decomposed by acids (including the carboxylic



(XXIV.)



(XXV.)



(XXVI.)

and the sulphonic acid groups present in the molecule itself), and it seems to be a rule that copper cannot enter the inner-complex unless the carboxylic or the sulphonic acid groups are neutralised by copper atoms or other basic groups.

(3) *Benzeneazo-β-naphthol-6 : 8-disulphonic acid.* This azo-compound gave a red copper salt (XXV), which was very soluble in water. The barium salt was similar; both are octahydrated. The inner-complex salts have not yet been examined in detail.

(4) 4-*Sulphonaphthalene*-1 : 2-*diazo-oxide.* The hexahydrated brownish-purple copper salt of this light-sensitive diazo-compound was examined, since Battegay and Schmidt (*Bull. Soc. chim.*, 1927, **41**, 205) considered it to be a co-ordinated salt, although Schmidt and Maier (*Ber.*, 1931, **64**, 767) dissented. The salt had the properties of a simple copper salt (XXVI), and treatment with the reagents noted above failed to bring about inner co-ordination of the metal. This is not unexpected, since a co-ordinated copper compound would here necessarily be the salt of a diazonium hydroxide.

## Experimental.

(a) o-*Hydroxy-azo-compounds.*—[All copper derivatives as (I).] *o*-Hydroxyazobenzene, m. p. 83°, was prepared by Bamberger's method (*Ber.*, 1900, **33**, 1947, 3188), purified through its copper salt, and crystallised from alcohol. Its copper salt, prepared in alcoholic solution by means of cupric acetate, or cupric chloride and sodium ethoxide, formed silky brown needles from alcohol or benzene, m. p. 222° (corr.), or from pyridine (m. p. 223°) (Found : C, 63·0; H, 4·05; Cu, 13·85. Calc. : C, 62·95; H, 3·95; Cu, 13·85%). It was stable to cold alkali, but unstable to hot alkali, mineral acid, or aqueous sodium sulphide. We were unable to cause *p*-hydroxyazobenzene to combine with copper, nor could we obtain copper salts from either of the isomeric 2-hydroxy-5-methylazoxybenzenes.

2-Hydroxy-5-methylazobenzene, m. p. 107°, gave, with alcoholic copper acetate, the copper salt, which formed lustrous bronzed-brown needles, m. p. 232°, from benzene or alcohol (Found : Cu, 13·15. Calc. : Cu, 13·1%).

2-Hydroxy-5 : 5′-dimethylazobenzene, m. p. 95°, was light reddish-brown; its copper salt, prepared as above, formed purplish-brown needles, m. p. 225°, from xylene (Found : Cu, 12·85. Calc. : Cu, 12·4%).

Benzeneazo-β-naphthol gave its dark-maroon bronzed copper salt, m. p. 292°, crystallised from nitrobenzene, which did not combine with ammonia or pyridine (Found : Cu, 11·4. Calc. : Cu, 11·35%).

*m*-Tolylazo-β-naphthol formed red plates with golden lustre, m. p. 141—142°, from alcohol. With alcoholic cupric acetate it gave *cupric* m-*tolylazo*-β-*naphthoxide*, which formed light

red-brown needles, m. p. 240—241°, from alcohol (Found: C, 69·6; H, 4·7; Cu, 11·3. $C_{34}H_{26}O_2N_4Cu$ requires C, 69·7; H, 4·45; Cu, 10·85%).

(b) *Azobenzene*-o-*carboxylic Acid*.—The azo-compound, prepared from nitrosobenzene and methyl anthranilate (Freundler, *Bull. Soc. chim.*, 1907, **1**, 219), formed orange plates, m. p. 97—98° (Found: C, 68·95; H, 4·95. Calc. for $C_{13}H_{10}O_2N_2$: C, 69·05; H, 4·45%). The red acid of the literature contains an unidentified substance which forms bright red needles, m. p. 225—229°, from acetic acid (Found: C, 66·15; H, 4·5; N, 11·75%).

*Cupric azobenzene*-o-*carboxylate* was precipitated as a dark oil when the azo-compound (1·7 g.) in alcohol (20 c.c.) was treated with 0·15 N-sodium hydroxide (1 equiv.), and an aqueous solution of cupric chloride dihydrate (1·28 g.) slowly stirred in. It soon solidified and then crystallised from chloroform in bright green prisms of the *dihydrate* (VI), m. p. 141—144°, which retained the water when dried for a short time over phosphoric oxide (Found: C, 56·8; H, 4·2; Cu, 11·6. $C_{26}H_{18}O_4N_4Cu,2H_2O$ requires C, 56·75; H, 4·0; Cu, 11·6%); an air-dried sample gave the same analysis. The dihydrate was very sparingly soluble in water, and was somewhat soluble to greenish-yellow solutions in chloroform, benzene, and pyridine, with loss of water when the solutions were heated (change of colour), but the anhydrous substance did not crystallise; on exposure to air, the dihydrate slowly separated. The impure anhydrous substance, m. p. 120—126° (decomp.), was prepared as a yellow powder by dissolving the dihydrate in benzene, boiling the solution to expel water, and precipitating the salt with light petroleum (Found: C, 59·4; H, 4·15; Cu, 13·85. $C_{26}H_{18}O_4N_4Cu$ requires C, 60·75; H, 3·5; Cu, 12·4%); it was hygroscopic but was liable to become hydrolysed to the free azo-compound and copper hydroxide. The dihydrate was completely hydrolysed on solution in glacial acetic acid and addition of water. Crystallised from aniline, the dihydrate gave a *dianiline* compound, yellowish-brown needles, m. p. 142° (Found: C, 65·45; H, 4·8; Cu, 9·65. $C_{26}H_{18}O_4N_4Cu,2C_6H_5{\cdot}NH_2$ requires C, 65·2; H, 4·6; Cu, 9·1%). From pyridine, in which it dissolved very readily, the dihydrate gave minute olive-green plates, m. p. 145—148° (decomp.), which still had a faint odour of pyridine after exposure to air for 18 hours; this appeared to be a *tripyridine* compound (Found: C, 65·65; H, 4·4; N, 13·35; Cu, 8·6. $C_{26}H_{18}O_4N_4Cu,3C_5H_5N$ requires C, 65·55; H, 4·4; N, 13·05; Cu, 8·5%); on being kept until all odour of pyridine was absent, the above gave a *dipyridine* compound (Found: C, 64·4; H, 4·8. $C_{26}H_{18}O_4N_4Cu,2C_5H_5N$ requires C, 64·3; H, 4·2%), which lost all its pyridine in 1 hour in a stream of dry air at 105° (Found: loss, 23·5. Calc.: loss for $2C_5H_5N$, 23·5%). When the tripyridine compound was dissolved in chloroform, precipitation with light petroleum gave yellowish-green stout needles, m. p. 183—184° (decomp.), of what is probably a *hemipyridine* compound (Found: C, 61·7; H, 4·05; Cu, 11·45. $C_{26}H_{18}O_4N_4Cu,\frac{1}{2}C_5H_5N$ requires C, 61·85; H, 3·7; Cu, 11·5%).

The *monoacetone* compound (VIII) separated from a solution of the dihydrate in acetone, as brownish-green hexagonal plates, m. p. 142° (decomp.) [Found: C, 60·55; H, 4·5; Cu, 11·15 $C_{26}H_{18}O_4N_4Cu,(CH_3)_2CO$ requires C, 60·9; H, 4·2; Cu, 11·1%]; this substance slowly los acetone at 115° (Found: loss, 8·5. Calc.: loss, 10·2%).

(c) *Azobenzene*-2 : 2′-*dicarboxylic Acid*.—The azo-compound was prepared by reducin o-nitrobenzoic acid (Griess, *Ber.*, 1877, **10**, 1869) and purified through the barium salt: i formed orange crystals, m. p. 238—239° (Found: C, 62·35; H, 3·9. Calc.: C, 62·2; H, 3·7%)

*Cupric azobenzene*-2 : 2′-*dicarboxylate* was obtained, by the interaction in aqueous solution c cupric chloride and the sodium salt of the azo-compound, as bright green micro-needles, sparingl soluble in water and almost insoluble in benzene; analyses for the air-dried substance wer inexact, but indicated a dihydrate. This salt, when dried at 110°, retained, or rapidly r absorbed from the air, 1 mol. of water, the *monohydrate* (IX) being stable in air (Found: ( 48·3; H, 3·5; Cu, 18·15. $C_{14}H_8O_4N_2Cu,H_2O$ requires C, 48·05; H, 2·85; Cu, 18·2%); decomposed at a higher temperature or when heated with water; mineral acids or aqueo sodium bicarbonate decomposed it, and potassium iodide or ferrocyanide gave reactions as f cupric ions. When freshly crystallised from pyridine, in which it was only moderately solubl it gave a green crystalline powder, probably a tripyridine-monohydrate, which lost pyridi slowly in air, becoming probably a monopyridine-monohydrate; the latter was soluble in boili water without decomposition, but liberated pyridine on addition of sodium carbonate. Analys for the last two complexes were inexact, owing to the instability of the pyridine compounc

(d) o-*Hydroxy*-o′-*carboxy-azo-compounds*.—o-Carboxybenzeneazo-*p*-cresol, dark-red crysta m. p. 186°, gave with boiling alcoholic cupric chloride the purplish red-brown *cupric* derivati (as X), which was purified by extraction with hot alcohol to remove free azo-compound (Foun C, 52·9; H, 3·7; Cu, 19·45. $C_{14}H_{10}O_3N_2Cu$ requires C, 52·9; H, 3·15; Cu, 20·0%); it w insoluble in benzene or alcohol, but soluble in aniline or pyridine. From the former it gave t

*monoaniline* compound as brown needles with faint green reflex (Found: C, 58·55; H, 4·5; Cu, 15·4. $C_{14}H_{10}O_3N_2Cu,C_6H_5·NH_2$ requires C, 58·45; H, 4·15; Cu, 15·5%); and from pyridine, a mouopyridine compound, brown needles, for which an inexact analysis was obtained owing to its tendency to lose pyridine.

*o*-Carboxybenzeneazo-β-naphthol formed bright red needles, m. p. 268° (decomp.), from nitrobenzene, and gave, as in the preceding case, the *copper* derivative (X) in brown needles with strong green reflex (Found: C, 57·95; H, 3·15; Cu, 17·9; *M*, in boiling pyridine, 328, 385, 347. $C_{17}H_{10}O_3N_2Cu$ requires C, 57·7; H, 2·85; Cu, 18·0%; *M*, 353·6), soluble in aniline or pyridine, but sparingly soluble in alcohol and insoluble in water. The *monoaniline* compound (XI), a brown powder, was prepared as before (Found: C, 62·2; H, 4·15; Cu, 14·45. $C_{17}H_{10}O_3N_2Cu,C_6H_5·NH_2$ requires C, 61·8; H, 3·8; Cu, 14·25%), and also the *monopyridine* complex, brown needles (Found: C, 60·95; H, 3·75; Cu, 14·8. $C_{17}H_{10}O_3N_2Cu,C_5H_5N$ requires C, 61·05; H, 3·45; Cu, 14·7%).

The action of cupric acetate on the azo-compound gave a brown basic copper derivative for which analyses (Found: C, 45·15; H, 3·25; Cu, 28·0%) indicated the formula $C_{17}H_{10}O_3N_2Cu,Cu(OH)_2$; this gave the same derivatives as the foregoing with aniline and pyridine.

(e) Benzeneazo-β-naphthol-3′-carboxylic acid, which formed a dark scarlet powder, m. p. 236—239°, from alcohol, gave with alcoholic cupric chloride (½ mol.), on gradual addition of aqueous sodium hydroxide (1 mol.), a brown precipitate of the normal copper carboxylate, but this was contaminated with cupric hydroxide; recrystallisation from pyridine gave a pure dipyridine compound (see below), but when the pyridine was removed by boiling with water hydrolysis again occurred, an impure salt being again obtained (Found: C, 61·8; H, 3·7; Cu, 10·4. $C_{34}H_{22}O_6N_4Cu$ requires C, 63·2; H, 3·4; Cu, 9·85%). Recrystallisation of the salt from aniline gave reddish-brown needles containing 3 or 4 aniline molecules, two of which appeared to be more firmly combined, but analyses varied with the method of drying (*e.g.*, a sample heated at 110° gave C, 66·85; H, 4·75; Cu, 7·65; whereas a sample dried over sulphuric acid gave C, 67·7; H, 5·15; Cu, 6·7. $C_{34}H_{22}O_6N_4Cu,2C_6H_5·NH_2$ requires C, 66·4; H, 4·4; Cu, 7·65%. $C_{34}H_{22}O_6N_4Cu,3C_6H_5·NH_2$ requires C, 67·5; H, 4·65; Cu, 6·85%).

The *dipyridine* compound separated slowly from a solution of the copper salt in pyridine; two forms were obtained: (i) (possibly XV) massive brown crystals with strong green reflex, m. p. 115—120° (Found: C, 65·45; H, 4·65; Cu, 7·1%), and (ii) (possibly XIV) golden-orange needles, m. p. 233—234° (darkening at 170°) (Found: C, 65·75; H, 4·45; Cu, 7·9. $C_{34}H_{22}O_6N_4,2C_5H_5N$ requires C, 65·7; H, 4·0; Cu, 7·9%). Both forms evolved pyridine when boiled with water. With alcoholic cupric acetate the azo-compound gave a brown powder which appeared from analysis to consist of the impure, partly co-ordinated copper salt, $C_{34}H_{20}O_6N_4Cu_2$ (Found: Cu, 20·5%), insoluble in water or benzene but soluble in and combining with pyridine or aniline; the solution of this substance in hot aniline deposited, on cooling, an amorphous brown powder (Found: C, 63·6; H, 4·6; N, 10·4; Cu, 13·05%) which may have been the compound $[C_{34}H_{20}O_6N_4Cu][Cu(C_6H_5·NH_2)_4]$ contaminated with copper oxide.

(f) Benzeneazo-α-naphthol-2′-carboxylic acid, which formed purplish-red crystals, m. p. 245—246°, from acetic acid, was purified throngh its sodium salt. The addition of an equivalent of aqueous sodium hydroxide to a solution of the azo-componnd (1 g.) and cupric chloride dihydrate (0·3 g.) in boiling alcohol (500 c.c.) gave brownish-red *cupric benzeneazo-α-naphthol-2′-carboxylate*, obtained as the dihydrate (as VI) after drying at 105° (Found: C, 59·85; H, 3·6; Cn, 9·6. $C_{34}H_{22}O_6N_4Cu,2H_2O$ requires C, 59·85; H, 3·6; Cu, 9·35%); this was insoluble in most solvents, but dissolved in hot aniline, the *anhydrous salt* (probably as VII *A*) separating as a brown powder (Found: C, 63·5; H, 4·0; Cu, 10·65. $C_{34}H_{22}O_6N_4Cu$ requires C, 63·2; H, 3·4; Cu, 9·85%). From pyridine, it separated in reddish-brown needles, m. p. 199°, of the *dipyridine compound* (Found: C, 65·85; H, 4·5; Cu, 8·05. $C_{34}H_{22}O_6N_4Cu,2C_5H_5N$ requires C, 65·7; H, 4·0; Cu, 7·9%); this lost the pyridine when boiled with water, giving the *trihydrate* of the above copper salt (Found: C, 58·55; H, 4·1; Cu, 9·4. $C_{34}H_{22}O_6N_4Cu,3H_2O$ requires C, 58·3; H, 4·0; Cu, 9·1%), which was converted into the dihydrate at 105° (Found: loss, 2·05. Calc. for loss of 1 $H_2O$, 2·55%).

(g) *oo′-Dihydroxy-azo-compounds.*—2 : 2′-Dihydroxyazobenzene, brownish-yellow plates, m. p. 171—172°, was prepared by fusing *o*-nitrophenol with potassium hydroxide (Willstätter and Benz, *Ber.*, 1906, **39**, 3492); Hunter and Barnes (J., 1928, 2051) regard this as the *trans*-form. The *copper* derivative (XVII) was obtained as a brown gelatinous precipitate when the azo-compound was treated with an excess of cupric acetate or chloride in alcoholic solution; it separated from aniline in copper-coloured needles, m. p. 346—347° (decomp.) (Found: C,

52·15; H, 3·45; Cu, 22·9. $C_{12}H_8O_2N_2Cu$ requires C, 52·25; H, 2·9; Cu, 23·1%). The ***mono-pyridine*** compound formed brown micro-needles with greenish lustre, becoming discoloured above 205° and blackening at 323° (Found: Cu, 18·05. $C_{12}H_8O_2N_2Cu,C_5H_5N$ requires Cu, 17·95%). The *monoquinoline* compound formed brown needles (Fouud: C, 62·45; H, 3·95; Cu, 16·2. $C_{12}H_8O_2N_2Cu,C_9H_7N$ requires C, 62·3; H, 3·7; Cu, 15·7%).

*o*-Hydroxybenzeneazo-β-naphthol was prepared from *o*-aminophenol and β-naphthol; it separated in bronzed-violet plates, m. p. 192°, from alcohol. The *copper* derivative (as XVII) separated from aniline in reddish-brown needles, stable and unmelted at 365° (Found: C, 58·85; H, 3·35; Cu, 19·6; *M*, in boiling pyridine, 336, 318. $C_{16}H_{10}O_2N_2Cu$ requires C, 58·95; H, 3·05; Cu, 19·55%; *M*, 325·6); it was decomposed by hydrochloric acid in presence of alcohol or ether, the azo-dye being recovered as red plates with greenish-gold lustre, m. p. 192°.

The *monopyridine* compound of the copper salt was purplish-red (green lustre), and decomposed above 200° (Found: C, 62·8; H, 4·1; Cu, 15·7. $C_{16}H_{10}O_2N_2Cu,C_5H_5N$ requires C, 62·3; H, 3·7; Cu, 15·6%); its pyridine was not lost at 110° in a stream of dry air, but was removed on boiling with alcohol.

The *monoquinoline* compound formed dark red needles with green lustre, decomposing above 200° (Found: Cu, 13·55. $C_{16}H_{10}O_2N_2Cu,C_9H_7N$ requires Cu, 14·0%).

Salicylidene-*o*-aminophenol (orange-red needles, m. p. 183°) gave with alcoholic cupric acetate the pale green *cupric* derivative (XIX), insoluble in water or benzene (Found: Cu, 23·6. $C_{13}H_9O_2NCu$ requires Cu, 23·15%); it crystallised in green needles from dimethylaniline, and dissolved to brownish-yellow solutions in pyridine, piperidine, and aniline.

(h) m-*Hydroxybenzeneazo*-β-*naphthol* was prepared from *m*-aminophenol and β-naphthol, as a reddish-brown powder, m. p. 231—233°, which may perhaps be a hemihydrate (Found: C, 70·5, 70·3; H, 4·7, 5·25. $C_{16}H_{12}O_2N_2,\frac{1}{2}H_2O$ requires C, 70·3; H, 4·85%). Its alcoholic solution was treated with cupric acetate, and water added; a dark brown precipitate was then obtained; this was extracted with boiling alcohol. The concentrated extract gave the *copper* derivative (XXI) as dark brown needles with strong green reflex, m. p. 237° to 244° according to the rate of heating; it was rather soluble in organic solvents; analysis of two preparations (Found: C, 62·05, 61·95; H, 4·8, 4·9; Cu, 10·55, 10·65. $C_{32}H_{22}O_4N_4Cu,1\frac{1}{2}H_2O$ requires C, 62·25; H, 4·05; Cu, 10·3%) showed that one copper atom was present to 32 carbon atoms, but the degree of hydration remained uncertain.

(i) *Azo-sulphonic Acids.*—Azobenzene-4-sulphonic acid was obtained as the trihydrate, orange plates, m. p. 130°, from water. An aqueous solution of the acid reacted with cupric chloride to give the sparingly soluble *pentahydrate* of the cupric salt in orange-yellow plates (Found: C, 42·4; H, 4·55; Cu, 9·5. $C_{24}H_{18}O_6N_4S_2Cu,5H_2O$ requires C, 42·65; H, 4·15; Cu, 9·4%). This separated from pyridine in yellowish-brown crystals, which, when dried in air for a day, appeared to be a *tripyridine* compound (Found: C, 56·8; H, 4·75; Cu, 7·95. $C_{24}H_{18}O_6N_4S_2Cu,3C_5H_5N$ requires C, 56·9; H, 4·0; Cu, 7·75%). If moisture was excluded, a pyridine solution, treated with benzene, gave brown hexagonal plates of an unstable penta- or hexa-pyridine compound (Found: C, 59·5; H, 4·95; N, 13·9; Cu, 5·8%); but if the benzene was moist, a substance containing both water and pyridine molecules was obtained (Found C, 55·85; H, 4·95; N, 11·5; Cu, 6·25%). When exposed to moist air, the pyridine compound all slowly revert to the pentahydrate. The addition of pyridine to a hot aqueous solution of th latter gave an insoluble yellow basic salt.

Benzeneazo-β-naphthol-4′-sulphonic acid was obtained from its sodium salt ("Orange II" in dark red needles, m. p. 139—140°. The *cupric* salt, prepared as above, formed light reddisb orange needles of the ***heptahydrate***, soluble in hot water (Found: C, 45·7; H, 4·65; Cu, 7·6 $C_{32}H_{22}O_8N_4S_2Cu,7H_2O$ requires C, 45·5; H, 4·25; Cu, 7·55%); it lost $5H_2O$ (Found: los 10·9. Calc., 10·65%) when dried over phosphoric oxide in a vacuum, giving the hygroscop brown *dihydrate* (Found: C, 50·9; H, 3·95; Cu, 9·2. $C_{32}H_{22}O_8N_4S_2Cu,2H_2O$ requires 50·95; H, 3·45; Cu, 8·45%). When the heptahydrate or the dipyridine pentahydrate (belo was dissolved in pyridine, and benzene added, golden-red needles of a ***tetrapyridine trihydra*** were obtained (Found: C, 57·5; H, 4·45; N, 10·15; Cu, 6·05. $C_{32}H_{22}O_8N_4S_2Cu,4C_5H_5N,3H_2$ requires C, 57·35; H, 4·4; N, 10·3; Cu, 5·85%).

The ***dipyridine pentahydrate***, which is soluble in water without loss of pyridine, was obtain in lustrous orange needles by dissolving the copper salt (0·25 g.) and the free acid (0·2 g.) in b water (15 c.c.), adding an excess of pyridine, and concentrating the solution to 5 c.c. (Foun C, 52·9; H, 4·6; N, 8·2; Cu, 6·65. $C_{32}H_{22}O_8N_4S_2Cu,2C_5H_5N,5H_2O$ requires C, 52·2; H, 4· N, 8·7; Cu, 6·6%).

Formation of inner co-ordinated complexes occurred in the following circumstances:

When pyridine was added to an aqueous solution of the simple cupric salt, purplish-brown microcrystals separated; these were recrystallised from water containing a little pyridine (Found : C, 50·45; H, 4·15; N, 9·15; Cu, 12·35. $[C_{32}H_{20}O_8N_4S_2Cu][Cu(C_5H_5N)_2(H_2O)_2],3H_2O$ requires C, 50·1; H, 4·05; N, 8·35; Cu, 12·65%). The *substance* may be regarded as (XXIV) in which $R_2$ is a cupric ion associated with two pyridine and two water molecules. The mother-liquor gave the simple cupric dipyridine pentahydrate of the azo-dye (above) and the copper-free orange-red pyridinium salt of the azo-dye. (ii) When aqueous cupric acetate was added to an aqueous solution of the simple cupric salt, dark purplish-brown micro-needles (reddish-brown streak) of the inner-complex salt (XXIV; $R_2$ = Cu) separated as the hexa- or hepta-hydrate (Found : C, 43·05, 44·1; H, 3·75, 4·1; Cu, 14·8, 13·85. $[C_{32}H_{20}O_8N_4S_2Cu]Cu,6H_2O$ requires C, 43·3; H, 3·6; Cu, 14·35; whereas the heptahydrate requires C, 42·8; H, 3·75; Cu, 14·05%); it was very sparingly soluble in water and insoluble in most organic solvents, but soluble in aniline, pyridine, and benzonitrile; it was decomposed by acids, but reacted only slowly with the common reagents for copper. (iii) The action of an excess of sodium acetate or sodium bicarbonate on a solution of the simple cupric salt gave a brown amorphous solid, readily soluble in water (Found : Cu, 7·3, 7·5%); this was probably (XXIV; R = Na). (iv) When a solution of the simple cupric salt (0·5 g.) in water (25 c.c.) was treated with a concentrated aqueous solution of ammonium acetate (2—3 g.), deep brown, rectangular prisms of the *ammonium* salt of the cupric complex (XXIV; R = $NH_4$) separated, probably as the *hexahydrate* (Found : C, 44·85; H, 5·05; Cu, 7·15. $[C_{32}H_{20}O_8N_4S_2Cu](NH_4)_2,6H_2O$ requires C, 44·65; H, 4·65; Cu, 7·4%). (v) When the simple cupric salt was dissolved in hot water and treated with dilute aqueous ammonia, a sparingly soluble, brown copper derivative was precipitated, and a similar substance was obtained by the action of copper acetate and ammonia on the free azo-dye (Found : C, 43·2; H, 4·35; Cu, 14·9%); this substance may be an ammino-analogue of the pyridino-compound described in (i).

Benzeneazo-β-naphthol-8-sulphonic acid, crystallised from alcohol and concentrated hydrochloric acid, formed deep reddish-purple needles with strong green reflex, m. p. 202° (decomp.). The simple *cupric* salt was a *tetrahydrate*, a bright red, crystalline powder (Found : C, 48·95; H, 4·0; Cu, 7·8. $C_{32}H_{22}O_8N_4S_2Cu,4H_2O$ requires C, 48·65; H, 3·8; Cu, 8·05%), which lost $2H_2O$ on being dried over phosphoric oxide (Found : loss, 4·85. Calc., 4·55%); crystallisation of this salt from pyridine with addition of benzene gave deep red, rhombic plates of the *tetrapyridine* derivative (Found : C, 60·6; H, 4·6; Cu, 6·0. $C_{32}H_{22}O_8N_4S_2Cu,4C_5H_5N$ requires C, 60·4; H, 4·05; Cu, 6·15%). Brown salts containing copper in the inner-complex condition are produced by acting upon an aqueous solution of the simple salt with sodium acetate (Found : Cu, 7·75%) or cupric acetate (Found : Cu, 14·15%).

2-Hydroxy-5-methylazobenzene-4′-sulphonic acid was prepared as the yellow sodium salt (hydrated), which crystallised from hydrochloric or acetic acid without loss of the metal. The simple *cupric* salt crystallised from water in flat brownish-orange needles of the hexa- or hepta-hydrate (Found : C, 41·05; H, 4·65; Cu, 8·1, 8·35. $C_{26}H_{22}O_8N_4S_2Cu,6H_2O$ requires C, 41·4; H, 4·5; Cu, 8·45%. $C_{26}H_{22}O_8N_4S_2Cu,7H_2O$ requires C, 40·45; H, 4·65; Cu, 8·25%). Dried over phosphoric oxide, it gave the dark brown *trihydrate* (Found : C, 45·1; H, 4·0; Cu, 9·15; loss of $H_2O$, 9·0. $C_{26}H_{22}O_8N_4S_2Cu,3H_2O$ requires C, 44·6; H, 4·0; Cu, 9·1; loss of $4H_2O$ from heptahydrate, 9·35%). Sodium acetate gave an amorphous brown sodium salt of the inner-coordinated complex (Found : Cu, 7·4%), and ammonium acetate gave reddish-brown rhombic plates of the corresponding *ammonium cupric* salt (Found : C, 40·55; H, 4·9; Cu, 7·85, 8·2%), apparently a penta- or tetra-hydrate and soluble in water to a red solution.

2-Hydroxy-5-methylazobenzene-3′-sulphonic acid was prepared as its hydrated orange sodium salt, which separated from dilute hydrochloric acid in purplish flakes. The simple *cupric* salt crystallised from water in orange-red plates, with golden lustre, of the *heptahydrate* (Found : C, 39·95; H, 4·9; Cu, 8·65. $C_{26}H_{22}O_8N_4S_2Cu,7H_2O$ requires C, 40·45; H, 4·65; Cu, 8·25%). Sodium acetate gave an amorphous brown sodium cupric salt (Found : Cu, 7·65%), and ammonium acetate gave a crystalline salt.

2-Hydroxy-α-azonaphthalene-4′-sulphonic acid, which formed purplish-red needles from alcohol and hydrochloric acid, gave the simple *cupric* salt in purplish-brown needles, sparingly soluble in water (Found, in two preparations : C, 50·1, 50·75; H, 4·8, 4·45; Cu, 7·8, 8·6%), indicating a hepta- or an octa-hydrate. With this salt sodium acetate gave a purplish-brown sodium cupric salt containing two sodium atoms to each copper atom (Found: Cu, 6·3; Na, 4·8%).

*Benzeneazo-β-naphthol-6 : 8-disulphonic* acid formed deep red needles, with green reflex. Its *barium* salt formed red needles, with greenish-gold reflex, of the *octahydrate* (Found : Ba, 19·8. $C_{16}H_{10}O_7N_2S_2Ba,8H_2O$ requires Ba, 20·0%); and its simple *cupric* salt formed red

needles, also an *octahydrate* (Found: C, 31·3; H, 4·35; Cu, 10·3. $C_{16}H_{10}O_7N_2S_2Cu,8H_2O$ requires C, 31·3; H, 4·25; Cu, 10·35%). The brown inner-co-ordinated salts were not examined.

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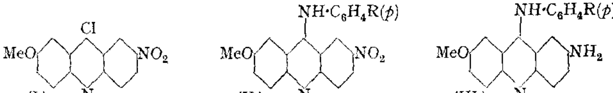
## 60. *Acridine Derivatives. Part I.*

By MOTI LAL DHAR, KARTAR S. NARANG, and JNANENDRA N. RAY.

Some 5-substituted 3-amino-7-methoxyacridines have been synthesised with the object of ascertaining their antiseptic activity.

IN view of the fact that the diaminoacridines possess bactericidal properties, it was thought interesting to synthesise acridines with an anilino- or substituted anilino-group in position 5 and an amino-group in one of the aromatic rings. For this purpose, 2-chloro-5-nitrobenzoic acid was condensed with *p*-anisidine and the 4-nitro-4′-methoxydiphenylamine-2-carboxylic acid thus formed was cyclised with phosphoryl chloride to 5-chloro-3-nitro-7-methoxyacridine (I). Magidson and Grigorowsky (*Ber.*, 1936, **69**, 404) prepared




(I.) (II.) (III.)

the diphenylaminecarboxylic acid in 33% yield, but under our conditions a yield of 60% is obtainable. We have also improved the preparation of the related chloroacridine. The above authors prepared 3-nitro-5-γ-diethylamino-β-hydroxypropylamino-7-methoxyacridine *via* the phenoxy-compound, but we found no difficulty in directly condensing (I) with *p*-anisidine, *p*-aminoacetanilide, *p*-phenetidine, *n*-butylamine, and piperidine in amyl-alcoholic solution. The products, of the type (II), were smoothly reduced to the corresponding amines (III) in most cases by the stannous chloride reagent described by Albert and Linnell (J., 1936, 1617).

The bactericidal properties (against *streptococci*) of these compounds are under examination.

### EXPERIMENTAL.

*4-Nitro-4′-methoxydiphenylamine-2-carboxylic Acid.*—A mixture of *p*-anisidine (6 g.) and 2-chloro-5-nitrobenzoic acid (5 g.) was stirred at 170—180° for 6—7 minutes and the dark mass thus obtained was triturated with dilute hydrochloric acid. The insoluble material crystallised from glacial acetic acid in bright yellow, parallelepiped plates (4·2 g.), m. p. 225° (Magidson and Grigorowsky give m. p. 216—220°) (Found: N, 9·7. Calc.: N, 9·5%).

*5-Chloro-3-nitro-7-methoxyacridine.*—The foregoing acid (1·0 g.) was heated with phosphoryl chloride (6 c.c.) at 110—115° for 45 minutes. The product, when cold, was washed with ligroin, and the residue treated with ice-cold 10% aqueous ammonia. The yellow substance was collected and stirred with cold acetone (12 c.c.); the insoluble portion crystallised from toluene in yellow plates (0·75 g.), m. p. 223° (Magidson and Grigorowsky give m. p. 220—221°) (Found: C, 58·4; H, 3·2; N, 9·9. Calc.: C, 58·2; H, 3·1; N, 9·7%).

*Condensation of 5-Chloro-3-nitro-7-methoxyacridine with* p-*Anisidine.*—A mixture of the acridine derivative (0·58 g.), *p*-anisidine (0·25 g.), and amyl alcohol (2·5 c.c.) was heated at 115—120° for 2 hours, an orange-coloured hydrochloride separating. After cooling, the mixture was diluted with light petroleum, and the precipitate collected and decomposed with aqueous ammonia. The liberated *3-nitro-5-*p*-anisidino-7-methoxyacridine*, isolated by means of ethyl acetate, crystallised from alcohol in bright scarlet needles, m. p. 212° (Found: N, 11·0. $C_{21}H_{17}O_4N_3$ requires N, 11·2%).

*Reduction.* The hydrochloride of the foregoing substance (1·0 g.) was gradually stirred int

the anhydrous stannous chloride reagent (30 c.c.; Albert and Linnell, *loc. cit.*, p. 1617). The mixture was left for 12 hours at 0°, and the precipitated tin double compound then collected and washed with acetic acid. Its carmine-red aqueous solution was basified, and extracted with chloroform. The well-washed chloroform solution was extracted with 1·5% hydrochloric acid (75 c.c.); the acid extract deposited orange-red needles of the amine hydrochloride, which could be recrystallised from water. It decomposed from 205° onwards. The 3-*amino*-5-p-*anisidino*-7-*methoxyacridine* liberated from the hydrochloride by aqueous ammonia crystallised from 5% aqueous alcohol in bright yellow needles, m. p. 182° (decomp.), which tenaciously retained water of crystallisation (Found for material dried at 140—150° in a high vacuum: N, 11·8. $C_{21}H_{19}O_2N_3$ requires N, 12·1%). Its *acetyl* derivative, prepared by means of warm acetic anhydride and acetic acid, crystallised from dilute alcohol in yellowish-orange needles, m. p. 258° (decomp.) (Found for material dried at 200° in a high vacuum for 2 hours: N, 10·9. $C_{23}H_{21}O_3N_3$ requires N, 10·85%).

3-*Nitro*-5-p-*phenetidino*-7-*methoxyacridine*.—The condensation of (I) (1·0 g.) and *p*-phenetidine (0·47 g.) in amyl alcohol (10 c.c.) at 120° for 3 hours furnished the *hydrochloride* of the above substance (1·3 g.), m. p. 281° (decomp.) (Found: N, 9·5. $C_{22}H_{19}O_4N_3$,HCl requires N, 9·9%). The *base*, liberated with alcoholic ammonia, crystallised from dilute alcohol in thick plates, m. p. 181°, containing solvent of crystallisation (Found for material dried at 140—150° in a high vacuum for 6 hours: N, 10·8. $C_{22}H_{19}O_4N_3$ requires N, 10·7%).

3-*Amino*-5-p-*phenetidino*-7-*methoxyacridine*.—The foregoing substance was reduced with the stannous chloride reagent. The *hydrochloride* of the base crystallised from 5% alcohol in sheaves of slender orange needles, m. p. (after drying in a high vacuum at 140°) 280° (decomp.) (Found: N, 9·5; HCl, 16·8. $C_{22}H_{21}O_2N_3$,2HCl requires N, 9·7; HCl, 16·9%). The *acetyl* derivative of the base crystallised from 50% alcohol in light orange needles, m. p. 235—237° (Found for material dried in a vacuum at 200° for 2 hours: N, 10·7. $C_{24}H_{23}O_3N_3$ requires N, 10·5%).

3-*Nitro*-5-*piperidino*-7-*methoxyacridine* was prepared in the manner already described. The scarlet-red solid formed was boiled with toluene (5 c.c.), and the residue crystallised from hot benzene; m. p. 220° (decomp.) (Found: N, 12·2. $C_{19}H_{19}O_3N_3$ requires N, 12·5%). The substance could not be reduced without decomposition.

3-*Nitro*-5-p-*acetamidoanilino*-7-*methoxyacridine* (II, R = NH·CO·$CH_3$).—*p*-Aminoacetanilide (0·26 g.) and (I) (0·5 g.) in amyl alcohol (10 c.c.) furnished the hydrochloride (0·6 g.), m. p. 287° (decomp.), after 4 hours' heating at 120°. The *base* crystallised from alcohol in dark red, rectangular plates, m. p. 270° (decomp.) (Found for material dried at 150° in a vacuum for 3 hours: N, 13·7. $C_{22}H_{18}O_4N_4$ requires N, 13·9%).

*Reduction.* A solution of the foregoing nitro-compound (1·0 g.) in alcohol (100 c.c.) and aqueous ammonia (*d* 0·88, 30 c.c.) was added to a boiling solution of ferrous sulphate (11·0 g.) in water (30 c.c.). After 1½ hours' heating, the solution was filtered, diluted with water (300 c.c.), and acidified with hydrochloric acid; the hydrochloride of 3-*amino*-5-p-*acetamidoanilino*-7-*methoxyacridine* slowly crystallised in long scarlet-red needles. The base crystallised from 30% alcohol in fine yellow needles, m. p. 279—280° (decomp.) (Found for material dried in a vacuum at 180° for 2 hours: N, 15·1. $C_{22}H_{20}O_2N_4$ requires N, 15·05%).

3-*Nitro*-5-*butylamino*-7-*methoxyacridine*.—A mixture of (I) (2·0 g.), *n*-butylamine (1·2 g.), and amyl alcohol (3 c.c.) was heated at 100° for 3 hours in a sealed tube. The product was diluted with light petroleum and the precipitate (2·1 g.) was collected and heated with alcoholic ammonia. The alcoholic solution, filtered hot, furnished on dilution an orange-red precipitate, which crystallised from 80% alcohol in long plates, m. p. 105°. The substance could not be satisfactorily dried without decomposition. The *hydrochloride* was prepared in alcoholic solution with concentrated hydrochloric acid and separated on standing; m. p. 242° (Found for material dried at 160—170° for 3 hours: N, 11·4; HCl, 9·75. $C_{18}H_{19}O_3N_3$,HCl requires N, 11·6; HCl, 10·1%).

The above compound was smoothly reduced by the "stannous chloride" reagent, but difficulty was experienced in crystallising the free base. It was purified *via* its hydrochloride, which crystallised readily in stout yellowish-orange prisms, m. p. 282°. The base was acetylated with acetic anhydride and acetic acid; 3-*acetamido*-5-*butylamino*-7-*methoxyacridine* crystallised from alcohol in yellow plates, m. p. 230° (Found for material dried at 170° for 2 hours: N, 12·6. $C_{20}H_{23}O_2N_3$ requires N, 12·5%).

The analyses recorded were all done by the micro-method.

The University, Lahore. [*Received, December 13th,* 1937.]

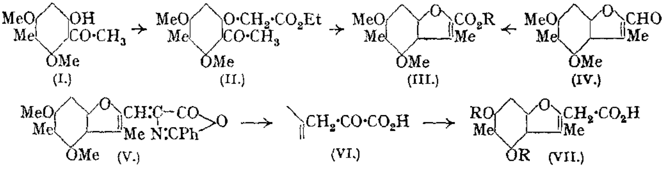
# 61. *Usnic Acid. Part VI. The Synthesis of O-Dimethylpyrousnic Acid.*

By Harold F. Birch and Alexander Robertson.

The observation that hydroxy- and methoxy-coumarones unsubstituted in the α-position yield α-formyl derivatives by the Gattermann reaction led to the preparation of 4 : 6-dimethoxy-2-formyl-3 : 5-dimethylcoumarone (IV), from which *O*-dimethylpyrousnic acid (VII) has been synthesised by the azlactone method, thereby confirming the constitution of pyrousnic acid, usnetic acid, and of decarbousnic acid. In order to test the method, the synthesis of 4 : 6-dimethoxy-3-methylcoumarone-2-acetic acid from the more accessible 4 : 6-dimethoxy-2-formyl-3-methylcoumarone was first studied. The orientation of the initial aldehydes has been conclusively established.

In Part IV (*J.*, 1936, 1834) indirect synthetical evidence was adduced in support of the formula (VII, R = H) for pyrousnic acid (Part III, *J.*, 1933, 1173; Asahina and Yanagita, *Ber.*, 1936, **69**, 1646), but since any formulation of usnic acid and of its main degradation products is primarily dependent on the structure of this compound (cf. Part V, J., 1937, 894, and Asahina and Yanagita, *loc. cit.*), it seemed highly desirable that the latter should be placed beyond doubt by a rational synthesis. This objective has now been achieved by the synthesis of *O*-dimethylpyrousnic acid according to a general method which depends on the observation that application of the Gattermann reaction to hydroxy- or methoxy-coumarones unsubstituted in the α-position leads to the formation of α-formyl derivatives (also unpublished work in this laboratory).

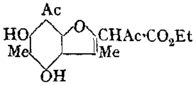
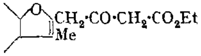
The *aldehyde* (IV) required for this synthesis was obtained in satisfactory yield from 4 : 6-dimethoxy-3 : 5-dimethylcoumarone and its orientation was established by the fact that on oxidation with potassium permanganate in aqueous acetone it gave rise to 4 : 6-*dimethoxy*-3 : 5-*dimethylcoumarone-2-carboxylic acid* (III, R = H), an authentic specimen of which was prepared from 2-*hydroxy*-4 : 6-*dimethoxy-5-methylacetophenone* (I) by way of the stages (II) and (III, R = Et). The ketone (I), which was obtained by isomerisation of the *acetate* of *C*-methylphloroglucinol β-dimethyl ether with aluminium chloride in nitrobenzene, could not be prepared by the condensation of *C*-methylphloroglucinol β-dimethyl ether and acetonitrile according to the method of Hoesch; in place of the expected ketimine a crystalline product was obtained which on hydrolysis regenerated the original phenol.



(I.) (II.) (III.) (IV.) (V.) (VI.) (VII.)

The pyruvic acid (VI) was formed by hydrolysis of the *azlactone* (V), obtained fron the aldehyde (IV) in the usual manner, and on oxidation with alkaline hydrogen peroxid gave rise to the acid (VII, R = Me), identical in every way with a natural specimen o *O*-dimethylpyrousnic acid. In consequence, pyrousnic acid is represented by formul (VII, R = H) and hence the structures of usnetic acid and of decarbousnic acid (Part V *loc. cit.*) are substantiated. In connection with the formation of the latter compoun from usnic acid it may be noted that by a similar procedure Asahina and his collaborato (*Proc. Imp. Acad. Tokyo*, **1937**, **33**, 270) have obtained an ester which, since it gave rise t acetic acid and usnetic acid or to carbon dioxide and deacetyldecarbousnic acid (Part V *loc. cit.*) on alkaline fission, they consider to have formula (VIII).

Further, these authors claim that the formation of (VIII) supports the pyronone structure for usnic acid. It must be observed, however, that the ester in question may be equally well represented by formula (IX), which on hydrolysis would be expected to give the same

(VIII.)   (IX.)

products as (VIII), and consequently the objections to the pyronone structure for usnic acid outlined in Part V (*loc. cit.*) must be maintained at present.

On account of the fact that 4 : 6-*dimethoxy-2-formyl-3-methylcoumarone* is considerably more accessible than the aldehyde (IV) and in order to test the method, we studied, in the first instance, the synthesis of 4 : 6-dimethoxy-3-methylcoumarone-2-acetic acid. The orientation of the initial aldehyde was established by the procedure employed for the homologue (IV).

## Experimental.

4 : 6-*Dimethoxy-3-methylcoumarone-2-carboxylic Acid.*—This was prepared in satisfactory yield by the following modification of the procedure described by Kostanecki and Tambor (*Ber.*, 1909, **42**, 909), who obtained the compound in small yield. Interaction of 2-hydroxy-4 : 6-dimethoxyacetophenone (1·5 g.) and ethyl bromoacetate (1·6 g.) in boiling acetone (50 c.c.), containing potassium carbonate (1 g.), during 12 hours gave rise to ethyl 3 : 5-dimethoxy-2-acetylphenoxyacetate, which on isolation was warmed with alcoholic sodium ethoxide (from 0·09 g. of sodium and 5 c.c. of alcohol) on the steam-bath for 1 hour. Addition of water (75 c.c.) to the reaction mixture precipitated ethyl 4 : 6-dimethoxy-3-methylcoumarone-2-carboxylate, which separated from dilute alcohol in pale yellow needles (0·3 g.), m. p. 134°.

Acidification of the alkaline filtrate left on separation of the ester gave 4 : 6-dimethoxy-3-methylcoumarone-2-carboxylic acid, which formed colourless rods (0·9 g.), m. p. 242° (decomp.), from alcohol and was identical with the product obtained by hydrolysis of the ester with warm 10% aqueous-alcoholic sodium hydroxide for 1 hour (Found: C, 61·3; H, 5·2. Calc. for $C_{12}H_{12}O_5$: C, 61·0; H, 5·1%). On being warmed, the yellow solution of the acid in concentrated sulphuric acid became red and then deep red. With alcoholic ferric chloride the acid gave a red coloration, which appears to be due to the formation of a red ferric salt; the ester does not give a coloration.

3 : 5-*Dimethoxyphenoxyacetone.*—An ethereal solution of the product formed by the interaction of phloroglucinol dimethyl ether (15 g.) and chloroacetone (12 g.) in boiling acetone (225 c.c.), containing potassium carbonate (45 g.), during 3·5 hours was washed with 5% aqueous sodium hydroxide to remove unchanged phenol and then with water, dried, and evaporated. Distillation of the residue in a high vacuum gave the ketone as a pale yellow oil (10·3 g.), b. p. 127—132°/0·1 mm., the 2 : 4-*dinitrophenylhydrazone* of which separated from ethyl acetate in yellow needles, m. p. 152° (Found: C, 52·5; H, 4·6; N, 14·3. $C_{17}H_{18}O_7N_4$ requires C, 52·3; H, 4·6; N, 14·4%).

4 : 6-*Dimethoxy-2-formyl-3-methylcoumarone.*—Cyclisation of the foregoing ketone (1 g.) was effected with concentrated sulphuric acid (4 c.c.) at 0° during 5 minutes and the resulting 4 : 6-dimethoxy-3-methylcoumarone was precipitated with water (100 c.c.), isolated with ether, and purified by distillation in a vacuum, being obtained as a crystalline solid (0·3 g.), b. p. 100—102°/0·1 mm., m. p. 36°, identical in every respect with a specimen obtained by decarboxylation of 4 : 6-dimethoxy-3-methylcoumarone-2-carboxylic acid (Kostanecki and Tambor, *loc. cit.*).

A solution of the coumarone (1·8 g.) in ether (50 c.c.), containing hydrogen cyanide (0·4 c.c.), was saturated at 0° with hydrogen chloride and next day the dark green product was collected, well washed with ether to remove hydrogen chloride, and dissolved in water (50 c.c.). On being heated on the steam-bath for ½ hour, the green solution gradually became colourless and, on cooling, deposited the *aldehyde*, which formed colourless rods (0·9 g.), m. p. 155°, from alcohol (Found: C, 65·6; H, 5·5. $C_{12}H_{12}O_4$ requires C, 65·5; H, 5·5%). The 2 : 4-*dinitrophenylhydrazone* separated from much ethyl acetate in clusters of small red needles, m. p. 274° (Found: C, 54·1; H, 4·1; N, 13·7. $C_{18}H_{16}O_7N_4$ requires C, 54·0; H, 4·0; N, 14·0%).

Potassium permanganate (1·6 g.), dissolved in water (40 c.c.) at 45°, was gradually added to a solution of the aldehyde (1 g.) in acetone (25 c.c.) maintained at 50° and after having been kept at room temperature for 1 hour, the reaction mixture was cleared with sulphur dioxide. The resulting 4 : 6-dimethoxy-3-methylcoumarone-2-carboxylic acid was separated from a little unchanged aldehyde by means of aqueous sodium bicarbonate and then crystallised from alcohol, forming colourless needles (0·5 g.), m. p. 242° (decomp.), identical with an authentic specimen.

4 : *6-Dimethoxy-3-methylcoumarone-2-pyruvic Acid*.—An intimate mixture of the aforementioned aldehyde (0·6 g.), hippuric acid (1 g.), sodium acetate (0·6 g.), and acetic anhydride (3·7 c.c.) was heated on the steam-bath for 1·5 hours, and the cooled reaction mixture treated with 50% alcohol (10 c.c.). Next day the *azlactone* was collected and recrystallised from acetic acid–alcohol, forming bright orange-red rods, m. p. 183·5° (Found: C, 69·3; H, 5·1; N, 3·7. $C_{21}H_{17}O_5N$ requires C, 69·4; H, 4·7; N, 3·9%).

This product (4 g.) was refluxed with 10% aqueous sodium hydroxide (60 c.c.) for 5 hours, and the cooled solution diluted with water (50 c.c.) and saturated with sulphur dioxide. Next day the benzoic acid was separated, and the liquor digested with concentrated hydrochloric acid on the steam-bath for 3 hours. The pyruvic acid, which separated from the acidic liquor as a pale yellow, micro-crystalline powder (2·5 g.), formed small prisms, m. p. 213—214° (decomp.), from dilute methyl alcohol and on oximation in alkaline solution gave rise to the *oxime*, which separated from water in clusters of colourless tiny prisms, m. p. 153° (decomp.) (Found: N, 4·8. $C_{14}H_{15}O_6N$ requires N, 4·7%).

4 : *6-Dimethoxy-3-methylcoumarone-2-acetic Acid*.—30% Hydrogen peroxide (0·8 c.c.) was added dropwise to a solution of the foregoing pyruvic acid (0·5 g.) in 5% aqueous sodium hydroxide (10 c.c.), and 1 hour later the mixture was heated at 50° for 15 minutes, cooled, and saturated with sulphur dioxide. Crystallisation of the resulting precipitate from dilute alcohol gave the *acid* in colourless needles (0·4 g.), m. p. 148° (Found: C, 62·7; H, 5·7. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·6%). On being warmed, the yellow solution of the compound in sulphuric acid became deep red and then violet.

*2-Hydroxy-4 : 6-dimethoxy-5-methylacetophenone* (I).—Prepared by the pyridine–acetic anhydride method, the *acetate* of *C*-methylphloroglucinol β-dimethyl ether (Part IV, *loc. cit.*) separated from dilute alcohol in colourless prisms, m. p. 78·5° (Found: C, 62·9; H, 6·7. $C_{11}H_{14}O_4$ requires C, 62·9; H, 6·7%).

Aluminium chloride (1·64 g.) was added to a cooled solution of this acetate (2 g.) in nitrobenzene (8·2 g.) and 24 hours later the mixture was treated with ice-water, the product and nitrobenzene isolated by means of ether, the ethereal solution repeatedly extracted with 5% aqueous sodium hydroxide, and the combined extracts acidified with hydrochloric acid. On isolation with ether the product was dissolved in warm light petroleum (b. p. 60—80°) and, after cooling, the solution was filtered to remove a little *C*-methylphloroglucinol β-dimethyl ether and then evaporated. Distillation of the residue in a vacuum gave the *ketone* as a pale yellow oil (1·5 g.), b. p. 110—112°/0·2 mm., which gave a violet coloration with alcoholic ferric chloride (Found: C, 62·6; H, 6·7. $C_{11}H_{14}O_4$ requires C, 62·9; H, 6·7%). The 2 : 4-*dinitrophenylhydrazone* separated from benzene in brilliant red prisms, m. p. 205—206° (Found: C 52·6; H, 4·9; N, 14·4. $C_{17}H_{18}O_7N_4$ requires C, 52·3; H, 4·6; N, 14·4%).

4 : *6-Dimethoxy-3 : 5-dimethylcoumarone-2-carboxylic Acid* (III, R = H).—The product obtained by the interaction of the foregoing ketone (1·5 g.), ethyl bromoacetate (1·6 g.), and potassium carbonate (1 g.) in boiling acetone for 12 hours was warmed on the steam-bath with alcoholic sodium ethoxide (from 0·1 g. of sodium and 5 c.c. of alcohol) for 1 hour, and the resulting *ethyl* 4 : *6-dimethoxy-3 : 5-dimethylcoumarone-2-carboxylate* (III, R = Et) precipitated with water (75 c.c.). Recrystallised from dilute alcohol, this ester formed almost colourless prisms having a negative ferric reaction (0·2 g.), m. p. 110° (Found: C, 64·6; H, 6·( $C_{15}H_{18}O_5$ requires C, 64·7; H, 6·5%).

Acidification of the alkaline liquor left after separation of the ester furnished the *aci* which formed colourless slender rods (0·8 g.), m. p. 219—220° (decomp.), from dilute alcoh and gave a red ferric reaction similar to that observed in the case of 4 : 6-dimethoxy-3-methy coumarone-2-carboxylic acid (Found: C, 62·1; H, 5·6. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·6%

4 : *6-Dimethoxy-2-formyl-3 : 5-dimethylcoumarone* (IV).—The procedure employed for t preparation of 4 : 6-dimethoxy-3 : 5-dimethylcoumarone was similar to that described l Asahina and Yanagita (*Ber.*, **1937**, **70**, 68); the intermediate 3 : *5-dimethoxy-4-methylphenox* acetone gave a 2 : 4-*dinitrophenylhydrazone* which separated from ethyl acetate–alcohol slender orange needles, m. p. 198° (Found: N, 14·1. $C_{18}H_{20}O_7N_4$ requires N, 13·9%).

On hydrolysis with water (75 c.c.) on the steam-bath for ½ hour the dark green aldimine which was obtained by the interaction of the coumarone (2 g.) with hydrogen cyanide (0·6 c.c.) in ether (75 c.c.), saturated with hydrogen chloride, gave rise to the *aldehyde*, which formed *colourless prisms* (1·2 g.), m. p. 127°, from alcohol (Found : C, 66·8; H, 6·0. $C_{13}H_{14}O_4$ requires C, 66·7; H, 6·0%). The 2 : 4-*dinitrophenylhydrazone* separated from ethyl acetate in tiny red prisms, m. p. 252° (Found : N, 13·7. $C_{19}H_{18}O_7N_4$ requires N, 13·5%).

Oxidation of this aldehyde by the procedure employed for the lower homologue gave rise to 4 : 6-dimethoxy-3 : 5-dimethylcoumarone-2-carboxylic acid, m. p. 219·5° (decomp.), identical in every way with an authentic specimen.

4 : 6-*Dimethoxy*-3 : 5-*dimethylcoumarone*-2 *pyruvic Acid* (VI).—Prepared by the interaction of the foregoing aldehyde (0·6 g.), hippuric acid (1 g.), sodium acetate (0·6 g.), and acetic anhydride (3·7 c.c.), the *azlactone* (V) formed slender orange rods (0·8 g.), m. p. 205°, from acetic acid–alcohol [Found : OMe, 16·2; N, 3·8. $C_{20}H_{13}O_3N(OMe)_2$ requires OMe, 16·4; N, 3·7%]. The *pyruvic acid*, obtained by the hydrolysis of the azlactone (2 g.) with boiling 10% aqueous sodium hydroxide for 6 hours, was isolated in the usual manner and separated from dilute acetic acid as a *hydrate* in pale yellow prisms, m. p. 190° (decomp.) [Found : C, 58·3; H, 5·5. $C_{15}H_{16}O_6,H_2O$ requires C, 58·1; H, 5·8%. Found for a specimen dried in a high vacuum at 80° : OMe, 21·0. $C_{13}H_{10}O_4(OMe)_2$ requires OMe, 21·2%].

4 : 6-*Dimethoxy*-3 : 5-*dimethylcoumarone*-2-*acetic Acid* (O-*Dimethylpyrousnic Acid*) (VII, R = Me).—This was obtained by oxidation of the foregoing acid (0·3 g.) with alkaline hydrogen peroxide. It formed colourless prisms (0·1 g.), m. p. 126°, from aqueous methyl alcohol, undepressed by admixture with a natural specimen (*loc. cit.*) [Found : C, 63·6; H, 5·9; OMe, 23·4. Calc. for $C_{12}H_{10}O_3(OMe)_2$ : C, 63·6; H, 6·1; OMe, 23·5%].

We are indebted to the Department of Scientific and Industrial Research for a maintenance grant to one of us (H. B.).

UNIVERSITY OF LIVERPOOL. [*Received, January 19th*, 1938.]

## 62. *Rottlerin. Part II.*

By ALEXANDER MCGOOKIN, ALFRED B. PERCIVAL, and ALEXANDER ROBERTSON.

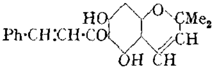
As the result of the re-examination of tetrahydrorottlerone and its derivatives, it has been shown that this compound and rottlerone have the empirical formulæ $C_{20}H_{22}O_4$ and $C_{20}H_{18}O_4$ respectively. Structural formulæ for rottlerone and its derivatives are deduced and a partial structure for rottlerin is tentatively suggested.

The formation of perhydrorottlerone by two methods has been re-investigated.

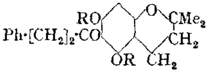
FROM the analytical results obtained for rottlerone and a number of its derivatives (Part I, J., 1937, 748), it appeared likely that this compound had the empirical formula $C_{20}H_{18}O_4$ or $C_{26}H_{24}O_5$ and since, on the basis of the formulæ * proposed for rottlerin heretofore, the rottlerone residue clearly constitutes the greater part of the rottlerin molecule, it seemed highly desirable to establish the structure of this important degradation product. Because of the difficulty of obtaining quantities of rottlerone, despite repeated attempts to improve the yield, we have concentrated our attention on the tetrahydro-derivative. As the result of the analysis of further specimens of this compound and of its dimethyl ether, in conjunction with the molecular weight determined by the *X*-ray method, it appears to be conclusively established that tetrahydrorottlerone has the empirical formula $C_{20}H_{22}O_4$ and that its acetyl and methyl derivatives are the diacetate $C_{20}H_{20}O_4(CO{\cdot}CH_3)_2$ and the dimethyl ether $C_{20}H_{20}O_2(OMe)_2$ respectively. This conclusion is in agreement with the fact that, in spite of a careful search, the only products obtained by the alkaline fission of tetrahydrorottlerone are 5 : 7-dihydroxy-2 : 2-dimethylchroman and β-phenylpropionic acid (compare Part I, *loc. cit.*). Consequently, rottlerone

* Perkin (J., 1895, **67**, 230), Hoffmann and Fari (*Arch. Pharm.*, 1933, **271**, 97), and Ray and co-workers (J., **1937**, **1862**) respectively have suggested the empirical formulæ $C_{33}H_{30}O_9$, $C_{31}H_{30}O_8$, and $C_{27}H_{26}O_7$. It may be noted here that the analytical data given in Part I (*loc. cit.*) are in close agreement with the formula $C_{30}H_{28}O_8$.

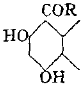
has the formula $C_{20}H_{18}O_4$, with which the analytical results stated in Part I (*loc. cit.*) are in good agreement, and further, in accordance with the arguments previously outlined (Part I), this compound, tetrahydrorottlerone, and *O*-dimethyltetrahydrorottlerone may be represented by formula type (I), (II, R = H), and (II, R = Me) respectively. In



(I.)

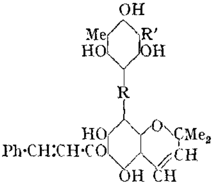


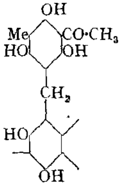
(II.)



(III.)

(IV.)





(V.)

this connexion, it may be noted that, since both rottlerone and its tetrahydro-derivative give strong ferric reactions in alcoholic solution, the acyl groups in these compounds are undoubtedly attached at either the 6- or the 8- position. Although direct experimental evidence on this point is lacking, the latter position appears to be excluded because compounds of the type (III) would be expected to dissolve readily in dilute aqueous sodium hydroxide, whereas both rottlerone and tetrahydrorottlerone are sparingly soluble in this reagent. In support of this conclusion, it may be recorded that 5 : 7-dihydroxy-8-acetyl-2 : 2-dimethylchroman is readily soluble in 4% aqueous sodium hydroxide (private communication from Mr. T. Backhouse of this laboratory).

In the formation of rottlerone and its hydrogenation products by means of alkalis we have found that small amounts of *C*-methylphloroglucinol are simultaneously produced (compare Part I) and, in agreement with this observation, Brockmann and Maier (*Naturwiss.*, 1937, **25**, 460) have recorded the formation of a derivative of *C*-methyl phloracetophenone from rottlerin. It may, therefore, be tentatively suggested that th rottlerin molecule is composed essentially of a rottlerone unit linked to a *C*-methylphloro glucinol residue, as in the structure type (IV) in which the nature of the radicals R an R′ cannot at present be clearly defined. Though the mode of union of the rottleron and the *C*-methylphloroglucinol units is not yet clear, it would appear from th comparative stability of rottlerin methyl ether towards alkalis (unpublished work) tha this linking is not of the ester or depside type (compare Part I). It may well be that ] is the radical $-CH_2-$, a view which would account for the production of *C*-dimethylphlor glucinol from rottlerin by means of zinc dust and boiling aqueous sodium hydroxide; tl possibility of an oxide link in addition to the carbon to carbon union of the *C*-methy phloroglucinol and rottlerone residues is also envisaged. Further, on the basis of a C formula for rottlerin in conjunction with the findings of Brockmann and Maier (*loc. cit.* the radical R′ may be $CH_3$·CO and hence rottlerin would have the structure type (V).

The preparation of perhydrorottlerone from rottlerin and from tetrahydrorottlero has been reinvestigated and the compound has now been found to melt at 147° and n at 178° as stated in Part I (*loc. cit.*).

## Experimental.

Rottlerone has been prepared by the following modification of the procedure employed Part I (*loc. cit.*). Saturated aqueous barium hydroxide (500 c.c.) was added to a solution rottlerin (20 g.) in pyridine (50 c.c.), and the well-stirred mixture heated at 75° for 5 minu

and rapidly cooled. The crimson solid which separated in the course of 24 hours was triturated with dilute acetic acid, and the friable product extracted with boiling ethyl acetate. On repeated crystallisation from methyl alcohol and then alcohol–chloroform, the residue gave rottlerone in characteristic garnet-red, pointed prisms (1 g.), m. p. 236°.

*Tetrahydrorottlerone*.—This compound has been prepared by the following improved method (compare Part I, *loc. cit.*). On being warmed, a solution of tetrahydrorottlerin (20 g.) in 8% aqueous sodium hydroxide (360 c.c.) became opaque at 63° and the mixture was then maintained at 63—70° for 20 minutes. The product, which separated on cooling, was collected and crystallised from acetone containing a little acetic acid and then from ethyl acetate, forming yellow prisms (5—6 g.), m. p. 172—173°, which gave a violet-green coloration with alcoholic ferric chloride (Found: C, 73·8; H, 6·7. Calc. for $C_{20}H_{22}O_4$: C, 73·6; H, 6·7%).

The buff precipitate obtained by acidification of the alkaline filtrate left on separation of the crude tetrahydrorottlerone was collected and triturated with aqueous sodium bicarbonate, aqueous sodium carbonate, water, and finally several times with cold methyl alcohol. On being kept, a solution of the resulting yellow resin in alcohol gradually deposited a further quantity of tetrahydrorottlerone, m. p. 172—173° after purification. Evaporation of the alcoholic washings and residues finally left much resinous material, from which crystalline material has not been obtained.

Extraction of the acidic filtrate from the buff precipitate with ether gave a small amount of a mixture of *C*-methylphloroglucinol and an unidentified phenol, m. p. 164°, which were separated by fractional sublimation in a high vacuum.

*O-Dimethyltetrahydrorottlerone*.—This has now been obtained more conveniently by the procedure first employed for the methylation of dehydrodihydrotoxicarol (J., 1937, 1535). A mixture of tetrahydrorottlerone (1 g.), methyl sulphate (5 c.c.), potassium carbonate (10 g.), and acetone (75 c.c.) was refluxed on the steam-bath for 2½ hours; after 2 hours, more sulphate (2·5 c.c.) and more carbonate (5 g.) were added. The reaction mixture was poured into water (200 c.c.) and the product, which solidified in the course of 2 hours, was collected next day and recrystallised from light petroleum (b. p. 60—80°), then aqueous alcohol, and finally methyl alcohol, forming colourless prisms, m. p. 101—102° [Found: C, 75·0; H, 7·4; OMe, 17·3, 17·4. Calc. for $C_{20}H_{20}O_2(OMe)_2$: C, 74·6; H, 7·4; OMe, 17·5%]. Oximation of this ether gave the oxime (Part I, *loc. cit.*), but attempts to obtain a 2 : 4-dinitrophenylhydrazone have been unsuccessful.

*Perhydrorottlerone*.—(A) Hydrogenation of tetrahydrorottlerin (1 g.) was effected in absolute alcohol (300 c.c.) in the presence of a platinum catalyst (0·15 g.) with hydrogen at 40 lb./sq. in. during 48 hours, and after the separation of the catalyst water was added until the solution became opalescent. The mixture was heated to 80° and on cooling deposited perhydrorottlerin in pale yellow needles, m. p. 185—187°, which, on repeated purification from ethyl acetate, aqueous alcohol, and finally benzene, had m. p. 188° and gave a purple-violet coloration with alcoholic ferric chloride (Found: C, 68·6; H, 7·2%). In the course of numerous experiments, a product was occasionally obtained which had m. p. 181—182°, unchanged on repeated purification. The direct hydrogenation of rottlerin with a platinum catalyst gave similar results. For the hydrogenation of rottlerin and its tetrahydro-derivatives with a platinum catalyst, ethyl acetate and acetone (compare Part I, *loc. cit.*) were found to be unsuitable as solvents, giving rise to impure products, and, when acetic acid was used, crystalline material could not be isolated from the product.

On being slowly heated, a solution of perhydrorottlerin (m. p. 188°) (2 g.) in 8% aqueous sodium hydroxide (40 c.c.) became opalescent at about 72—73°. The reaction mixture was kept at this temperature for 5 minutes and then rapidly cooled. Repeated crystallisation of the well-washed precipitate from alcohol or aqueous alcohol gave perhydrorottlerone in pale yellow prisms or plates (0·5 g.), m. p. 147°, which gave a violet coloration with alcoholic ferric chloride (Found: C, 73·2; H, 8·0%. Found for a specimen dried in a high vacuum at 80°: C, 73·0; H, 7·7%). A similar yield of the same product, m. p. 147°, was obtained from specimens of perhydrorottlerin, m. p. 181—182°.

Acetylation of perhydrorottlerone (0·5 g.) with acetic anhydride (12 c.c.) and pyridine (6 c.c.) on the water-bath for 15 minutes and then at room temperature for 14 days gave the *acetyl* derivative, which separated from acetone–alcohol in tiny colourless prisms, m. p. 206—207° (Found: C, 70·0; H, 7·0%).

In the course of many experiments on the preparation of perhydrorottlerin by the hydrogenation of rottlerin or tetrahydrorottlerin, we have observed that the melting point does not appear to be a safe criterion of the homogeneity of the product. The latter, however,

appears to be best tested by converting the material into perhydrorottlerone, m. p. 147°. Impure specimens of perhydrorottlerin, *e.g.*, m. p. 179°, arising from the use of an inefficient catalyst or an unsuitable solvent, furnished a mixed product from which, on several occasions, perhydrorottlerone, m. p. 147°, and tetrahydrorottlerone, m. p. 167°, could be isolated by a tedious fractional crystallisation.

(B) Hydrogenation of tetrahydrorottlerone (1 g.), dissolved in acetone (300 c.c.), with hydrogen at 40 lb./sq. in. and a platinum catalyst (0·1 g.) in the course of 44 hours gave rise to perhydrorottlerone (0·5 g.), m. p. 147° after recrystallisation from ethyl acetate, acetone, and finally alcohol. In the course of the purification of quantities of this compound from alcohol or ethyl acetate, a second form, pale yellow needles, m. p. 159—160°, was sometimes obtained. On further crystallisation from the same solvents, this material reverted to the form, m. p. 147°.

In several hydrogenation experiments the product appeared to be a mixture of perhydrorottlerone and unchanged material.

On account of the fact that tetrahydrorottlerone is sparingly soluble in cold acetic acid or alcohol, neither of these solvents was used as a medium for hydrogenation.

We are indebted to Dr. R. W. Roberts of the Department of Physics for the following summary of the data on tetrahydrorottlerone submitted by Mr. W. D. Goodman: The crystals of tetrahydrorottlerone are transparent yellow pinakoids belonging to the triclinic pinakoidal class; $\alpha = 153° 12'$, $\beta = 109° 6'$, $\gamma = 68° 48'$.

X-*Ray data*: $a = 11·01$ A., $b = 17·02$ A., $c = 21·69$ A. Space group $C_i^1$. Density 1·263 g. per c.c. With $M = 326·2$, the number of molecules in the unit cell is 4·03, *i.e.*, the unit cell must contain two non-equivalent sets of two asymmetric chemical molecules.

The authors gratefully acknowledge their indebtedness to the Government Grants Committee of the Royal Society for a grant in aid of this work, and to Professor Chadwick, Department of Physics, who provided facilities for carrying out the *X*-ray examination of tetrahydrorottlerone.

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## 63. *The Resolution of* n-*Propylpropenylcarbinol. The Refractivity and Optical Rotatory Dispersion of some Substituted Allyl Alcohols.*

By C. L. Arcus and J. Kenyon.

The resolution of *n*-propylpropenylcarbinol (γ-methyl-α-propylallyl alcohol) into its optically active forms, and the properties of some derivatives of the latter, are described.

Comparison of its molecular refractivity and optical rotatory dispersion is made with those of four other optically active substituted allyl alcohols. It is considered probable that these alcohols have the *trans*-configuration. Evidence is adduced that, although the optical rotatory dispersion of the purely alkyl-substituted allyl alcohols is complex, that of the phenyl-substituted allyl alcohols is simple, and it is suggested that a large proportion of the rotatory power of the latter group of compounds is due to induced dissymmetry of the phenyl radical.

Several investigations, dealing with the chemical and optical properties of optically active substituted allyl alcohols, which have arisen from the peculiar behaviour of αγ-dimethylallyl alcohol (I) (Hills, Kenyon, and Phillips, J., 1936, 576) have recently appeared [γ-phenyl-α-methylallyl alcohol (II), Kenyon, Partridge, and Phillips, *ibid.*, p. 85; α-phenyl-γ-methylallyl alcohol (III), *idem*, J., 1937, 207; αγγ-trimethylallyl alcohol (IV) Duveen and Kenyon, J., 1936, 1451] and in furtherance of these studies optically active *n*-propylpropenylcarbinol (γ-methyl-α-*n*-propylallyl alcohol) (V) has now been examined.

(I) CHMe:CH·CHMe·OH (II) CHPh:CH·CHMe·OH (III) CHMe:CH·CHPh·OH
(IV) $CMe_2$:CH·CHMe·OH (V) CHMe:CH·CHPr$^a$·OH

*dl*-*n*-Propylpropenylcarbinol has been described by Reif (*Ber.*, 1906, **39**, 1603) and the refractivity of a pure specimen was determined by Auwers and Westermann (*Ber.*, 192

54, 2993). A partial resolution of the alcohol by the fractional crystallisation of the brucine salt of its hydrogen phthalic ester was effected by Levene and Marker (*J. Biol. Chem.*, 1934, 106, 173), but the maximum rotatory power obtained was only some 8% of that now reported.

A satisfactory resolution by means of the brucine salt could not be effected, although several procedures were tried. Complete resolution was eventually obtained by fractional crystallisation from dry acetone of the strychnine salt of the hydrogen phthalic ester, followed by fractional crystallisation of the *d* + *dl*- and *l* + *dl*-esters obtained by decomposition of the less soluble and the more soluble fractions, respectively, of the strychnine salt. The *d*- and *l*-hydrogen phthalic esters, when hydrolysed with sodium hydroxide, yielded the corresponding optically active alcohols, the rotatory powers of which under different experimental conditions are recorded in Tables I, II, and III. The acetic and benzoic esters and the methyl ether of the *d* *-alcohol have been prepared and their rotatory powers are recorded in Tables V—VII.

As experiments are at present in progress on the replacement reactions of this alcohol and its esters whereby a rearrangement to the isomeric α-methyl-γ-*n*-propylallyl alcohol ($CHPr^{\alpha}{:}CH{\cdot}CHMe{\cdot}OH$) and its esters may occur, it was considered expedient to establish the homogeneity of the optically active alcohol and esters, since rearrangement may occur both during the production of the intermediate *dl*-hydrogen phthalic ester (Kenyon, Partridge, and Phillips, J., 1937, 207) and also during the esterification of the alcohol obtained therefrom by hydrolysis. Accordingly these substances were catalytically reduced; the optically active forms then yielded optically inactive di-*n*-propylcarbinol and its esters respectively, indicating the original substances to be free from structural isomerides.

*Optical Rotatory Dispersion of* n-*Propylpropenylcarbinol and its Derivatives.*—The optical rotatory dispersion of *n*-propylpropenylcarbiuol in the homogeneous state at 16° (Table I) may be represented, within the limits of experimental error, by the equation

$$\alpha = 1{\cdot}027/(\lambda^2 - 0{\cdot}0723)\,;\ \lambda_0 = 2690\ \text{A}.$$

The simplicity can only be apparent, for the rotatory dispersions of solutions of the alcohol show obvious complexity when $1/\alpha$ is plotted against $\lambda^2$ and the solution in benzene shows a reversal of sign of rotation (Table II).

TABLE I.

*Rotatory Powers of* (+)n-*Propylpropenylcarbinol at* 16° (l, 0·5).

| λ. | $\alpha_{obs.}$ | $\alpha_{calc.}$ | $\alpha_{obs.} - \alpha_{calc.}$ | λ. | $\alpha_{obs.}$ | $\alpha_{calc.}$ | $\alpha_{obs.} - \alpha_{calc.}$ |
|---|---|---|---|---|---|---|---|
| 6438 | +2·98° | +3·00° | −0·02° | 5086 | +5·48° | +5·51° | −0·03° |
| 5893 | 3·68 | 3·73 | −0·05 | 4800 | 6·40 | 6·49 | −0·09 |
| 5780 | 3·96 | 3·90 | +0·06 | 4678 | 6·82 | 7·00 | −0·18 |
| 5461 | 4·58 | 4·54 | +0·04 | 4358 | 8·76 | 8·73 | +0·03 |

TABLE II.

*Specific Rotatory Powers of* (+)n-*Propylpropenylcarbinol in Various Solvents at Room Temperature* (l, 2·0).

| Solvent. | *t*. | *c*. | $[\alpha]_{6438}$. | $[\alpha]_{5893}$. | $[\alpha]_{5461}$. | $[\alpha]_{4358}$. |
|---|---|---|---|---|---|---|
| Benzene | 19° | 4·830 | − 1·86° | − 0·21° | + 0·72° | + 2·69° |
| Chloroform | 20 | 5·245 | − 7·53 | − 7·72 | − 8·30 | −13·25 |
| Carbon disulphide | 21 | 5·935 | + 3·37 | + 6·24 | + 8·26 | +17·6 |
| Pyridine | 22 | 4·615 | +11·5 | +15·8 | +19·9 | +39·4 |

Furthermore, the magnitude of the rotatory power of the alcohol in the homogeneous state is much reduced with increase of temperature (Table III) and the dispersion ratio $\alpha_{4358}/\alpha_{5461}$ increases from 1·92 at 16° to 2·09 at 65° and to 2·24 at 95°, showing the sensitivity to temperature change (and solvent influence) associated with complex rotatory dispersion.

* In the introductory part of this communication rotatory powers are given for derivatives of the *d*(+)-alcohol, although in some cases the experimental data were determined by using derivatives of opposite configuration.

No evidence of mutarotation was observed and the alcohol retained its original rotatory power after being kept at 34—39° for 15 days.

TABLE III.

*Rotatory Power of* (+)n-*Propylpropenylcarbinol at Different Temperatures* (l, 0·5).

| $t$. | $\alpha_{5893}$. | $\alpha_{5461}$. | $\alpha_{4358}$. | $t$. | $\alpha_{5893}$. | $\alpha_{5461}$. | $\alpha_{4358}$. |
|---|---|---|---|---|---|---|---|
| 16° | +3·68° | +4·58° | +8·76° | 65° | +1·88° | +2·35° | +4·90° |
| 26 | 3·37 | 4·12 | 8·05 | 70 | 1·69 | 2·13 | 4·49 |
| 36·5 | 2·92 | 3·65 | 7·23 | 95 | 1·01 | 1·32 | 2·95 |
| 45·5 | 2·56 | 3·16 | 6·35 | 5 * | 4·22 | 5·13 | 9·69 |
| 54 | 2·23 | 2·83 | 5·66 | | | | |

* After cooling.

The rotatory powers of (+)*n*-propylpropenylcarbinyl hydrogen phthalate in various solvents (Table IV) indicate pronounced complex rotatory dispersion when $1/\alpha$ is plotted against $\lambda^2$; the corresponding benzoic ester in the homogeneous state (Table V) shows a slightly complex rotatory dispersion.

TABLE IV.

*Specific Rotatory Powers of* (+)n-*Propylpropenylcarbinyl Hydrogen Phthalate in Various Solvents at Room Temperature* (l, 2·0).

| Solvent. | $t$. | $c$. | $[\alpha]_{6438}$. | $[\alpha]_{5893}$. | $[\alpha]_{5780}$. | $[\alpha]_{5461}$. | $[\alpha]_{4358}$. |
|---|---|---|---|---|---|---|---|
| Alcohol .................. | 16° | 4·550 | +13·3° | +17·05° | — | +22·85° | +46·4° |
| Benzene .................. | 20 | 4·275 | — | + 6·67 | + 8·31° | + 9·59 | +23·0 |
| Chloroform ............... | 19 | 4·815 | — | + 4·26 | + 5·19 | + 6·33 | +17·4 |
| Carbon disulphide ...... | 20 | 4·38 | — | −14·7 | −15·2 | −16·8 | −32·0 |

TABLE V.

*Rotatory Power of* (+)n-*Propylpropenylcarbinyl Benzoate* (l, 0·5; t, 20°).

| $\lambda$ ........................ | 6438 | 5893 | 5780 | 5461 | 5086 | 4800 | 4678 | 4358 |
|---|---|---|---|---|---|---|---|---|
| $\alpha_{obs.}$ ...................... | +6·47° | +8·50° | +9·19° | +11·16° | +14·00° | +17·39° | +19·05° | +25·76° |

The rotatory dispersion of (−)*n*-propylpropenylcarbinyl acetate in the homogeneous state (Table VI) can, however, be accurately represented by the equation

$$\alpha = -6{\cdot}14/(\lambda^2 - 0{\cdot}0452),\quad \lambda_0 = 2120\ \text{A.}$$

It appears, therefore, that under these conditions the rotatory power is predominatingly dne to the induced dissymmetry of the $-C{<}^{O}_{O-}$ radical, which has an absorption band at 2100 A. (Lowry, "Optical Rotatory Power," 1935, p. 266).

TABLE VI.

*Rotatory Powers of* (−)n-*Propylpropenylcarbinyl Acetate in the Homogeneous State at* 21° (l, 0·5).

| $\lambda$. | $\alpha_{obs.}$ | $\alpha_{calc.}$ | $\alpha_{obs.} - \alpha_{calc.}$ | $\lambda$. | $\alpha_{obs.}$ | $\alpha_{calc.}$ | $\alpha_{obs.} - \alpha_{calc.}$ |
|---|---|---|---|---|---|---|---|
| 6438 | −16·52° | −16·64° | +0·12° | 5086 | −28·9° | −28·8° | −0·1° |
| 5893 | 20·35 | 20·33 | +0·02 | 4800 | 33·3 | 33·2 | −0·1 |
| 5780 | 21·25 | 21·26 | +0·01 | 4678 | 35·4 | 35·4 | ±0·0 |
| 5461 | 24·28 | 24·30 | +0·02 | 4358 | 42·4 | 42·4 | ±0·0 |

TABLE VII.

*Rotatory Powers of* (−)n-*Propylpropenylcarbinyl Methyl Ether at* 26° (l, 0·25).

| $\lambda$. | $\alpha_{obs.}$ | $\alpha_{calc.}$ | $\alpha_{obs.} - \alpha_{calc.}$ | $\lambda$. | $\alpha_{obs.}$ | $\alpha_{calc.}$ | $\alpha_{obs.} - \alpha_{calc.}$ |
|---|---|---|---|---|---|---|---|
| 6438 | − 8·14° | − 8·48° | +0·34° | 5086 | −13·55° | −13·83° | +0·28° |
| 5893 | − 9·89 | −10·2 | +0·31 | 4800 | −15·36 | −15·62 | +0·26 |
| 5780 | −10·98 | −10·6 | −0·38 | 4678 | −16·10 | −16·50 | +0·40 |
| 5461 | −12·00 | −11·92 | −0·08 | 4358 | −19·67 | −19·17 | −0·50 |

The rotatory dispersion of (—)*n*-propylpropenylcarbinyl methyl ether (Table VII) can be represented by a single-term Drude equation, $\alpha = -3{\cdot}42/(\lambda^2 - 0{\cdot}0113)$, but the small value of the dispersion constant, $\lambda_0^2 = 0{\cdot}0113$, raises a suspicion that two terms of opposite sign may be necessary to express the dispersion over a more extended range of observations.

*The Optical Properties of Substituted Allyl Alcohols.*—The investigations recorded in the first paragraph have been directed primarily towards the study of the reactions of optically active substituted allyl alcohols, but many optical data have also been recorded and some relationships are indicated below.

TABLE VIII.

*Molecular Refractivities.*

| Compound. | *t*. | $n_D^{t°}$. | $d_{4°}^{t°}$. | $[R]_D$ obs. | $[R]_D$ calc. |
|---|---|---|---|---|---|
| CHMe:CH·CHMe·OH * | 18° | 1·4282 | 0·8382 | 26·44 | 26·35 |
| CHMe:CH·CHPr$^\alpha$·OH * | 14·4 | 1·4397 | 0·8422 | 35·69 | 35·58 |
| $CMe_2$:CH·CHMe·OH | 17 | 1·4297 | 0·8461 | 30·51 | 30·97 |
| CHMe:CH·CHMe·OAc | 26 | 1·4143 | 0·8931 (at 25°) | 35·83 | 35·71 |
| CHMe:CH·CHPr$^\alpha$·OAc | 17 | 1·4270 | 0·8815 (at 20°) | 45·33 | 44·95 |

* Auwers and Westermann (*loc. cit.*). The calculated values are obtained by means of the constants of Eisenlohr (*Z. physikal. Chem.*, 1911, **75**, 605). In the last two examples, the densities are adjusted to the temperature at which the refractive index is determined (—0·0008 unit for +1°).

The agreement with the values calculated from the open-chain formulæ given above appears satisfactory.

In order to account for various reactions and for values in the observed parachors of αγ-dimethylallyl alcohol it was tentatively suggested that this substance might contain a large proportion of the isomeric inner ether, $\genfrac{}{}{0pt}{}{H}{Me}{>}C{<}\genfrac{}{}{0pt}{}{CH_2}{O}{>}C{<}\genfrac{}{}{0pt}{}{Me}{H}$. A compound of this constitution should have $[R]_D$ 25·21; analogous structures for the other alcohols in Table VIII would have values of $[R]_D$ lower by 1·14 units than those recorded (the value used for a four-membered ring is + 0·48, as determined by Östling; J., 1912, **101**, 457). It now appears that the ethylenic link cannot be absent and accordingly a formulation of these compounds is being developed in which the ethylenic character is distributed between the αβ- and the βγ-linkage.

*Geometrical Configurations.*—Alcohols (I), (II), (III), and (V) are considered to be *trans*-isomerides on the following evidence; (I), (III), and (V) are prepared by the interaction of the appropriate Grignard reagent and crotonaldehyde. This aldehyde, obtained by the dehydration of aldol, was found by Kaufler (*Monatsh.*, 1929, **53**, 119) to yield on oxidation principally crotonic acid (*trans*-), together with some *iso*crotonic acid; Blacet, Young, and Roof (*J. Amer. Chem. Soc.*, 1937, **59**, 608), however, have concluded that purified commercial crotonaldehyde consists solely of the *trans*-isomeride, since the ultra-violet absorption spectrum remains unaltered after the crotonaldehyde has been submitted to such treatment as would alter the ratio *cis*- to *trans*- if a certain proportion of the former isomeride were originally present. Alcohol (II) is prepared similarly from cinnamaldehyde, which also should possess the *trans*-configuration, since it is converted by aerial oxidation into cinnamic acid (*trans*-). None of the subsequent operations involved in the resolution of the hydrogen phthalic esters appears likely to cause geometrical inversion and no indications that these carbinols are mixtures of geometrical isomerides have appeared. The *d*- and the *l*-form of γ-phenyl-α-methylallyl alcohol are solids which crystallise readily from various solvents, but an exhaustive research failed to effect any separation.

*Rotatory Dispersion.*—The range of wave-lengths for which data are available may in some cases be too restricted for the detection of smaller deviations from simplicity of rotatory dispersion, but where the dispersion ratio $\alpha_{4358}/\alpha_{5461}$ remains insensitive to variations of temperature and solvent influence it may be concluded that the rotatory dispersion exhibits real simplicity. Alcohol (I) was demonstrated by Hills, Kenyon, and Phillips (*loc. cit.*) to possess a complex rotatory dispersion and this is shown above to apply also to alcohol (V). Alcohol (IV) in the homogeneous state shows a slight complexity of

rotatory dispersion when $1/\alpha$ is plotted against $\lambda^2$, and the dispersion ratio $\alpha_{4358}/\alpha_{5461}$ is little influenced by changes of temperature, as the following data show:

| | | | |
|---|---|---|---|
| $t$ | 20° | 50° | 76° |
| $\alpha_{4358}/\alpha_{5461}$ | 1·78 | 1·77 | 1·75 |

On the other hand, this dispersion is more susceptible to solvent influence:

| | | | |
|---|---|---|---|
| Solvent | $C_5H_5N$ | $CHCl_3$ | $Et_2O$ |
| $\alpha_{4358}/\alpha_{5461}$ | 2·21 | 1·64 | 1·90 |

and in pyridine solution the sign of rotation is reversed.

It thus appears that alcohol (IV) also possesses complex rotatory dispersion.

Unlike the saturated aliphatic secondary alcohols, which uniformly possess simple rotatory dispersions, the alkyl-substituted allyl alcohols hitherto examined all show complexity of rotatory dispersion. The rotatory dispersion of the semi-aromatic alcohol (II) can be represented by a single-term equation (Table IX):

$$\alpha = 4{\cdot}425/(\lambda^2 - 0{\cdot}0876);\ \lambda_0 = 2960\ \text{A.}$$

TABLE IX.

*Rotatory Powers of γ-Phenyl-α-methylallyl Alcohol* (t, 51°; l, 0·5).

| | | | |
|---|---|---|---|
| $\lambda$ | 5780 | 5461 | 4358 |
| $\alpha_{obs.}$ | 17·96° | 21·00° | 43·23° |
| $\alpha_{calc.}$ | 17·97° | 21·01° | 43·20° |
| $\alpha_{obs.} - \alpha_{calc.}$ | −0·01° | −0·01° | +0·03° |

The dispersion ratio is relatively insensitive to changes in temperature:

| | | |
|---|---|---|
| $t$ | 51° | 95° |
| $\alpha_{4358}/\alpha_{5461}$ | 2·06 | 2·00 |

and to the influence of solvents:

| | | | | |
|---|---|---|---|---|
| Solvent | $CS_2$ | $C_6H_6$ | $COMe_2$ | $CHCl_3$ |
| $\alpha_{4358}/\alpha_{5461}$ | 2·09 | 1·94 | 2·06 | 1·97 |

The largest deviation from the mean value is found in the benzene solution; the dispersion in this case may be represented, however, by a single-term equation (Table X):

$$\alpha = 4{\cdot}97/(\lambda^2 - 0{\cdot}0742);\ \lambda_0 = 2730\ \text{A.}$$

TABLE X.

*Rotatory Powers of γ-Phenyl-α-methylallyl Alcohol in Benzene Solution* (c, 4·070; l, 2).

| | | | | |
|---|---|---|---|---|
| $\lambda$ | 5893 | 5780 | 5461 | 4358 |
| $\alpha_{obs.}$ | +18·2° | +19·4° | +22·2° | +43·0° |
| $\alpha_{calc.}$ | +18·2° | +19·15° | +22·2° | +43·0° |
| $\alpha_{obs.} - \alpha_{calc.}$ | ± 0·0° | + 0·25° | ± 0·0° | ± 0·0° |

The numerical values of the rotatory powers in other solvents are not very different.

The rotatory dispersion of the isomeric alcohol (III) also can be represented by a single term equation (Table XI):

$$\alpha = -7{\cdot}73/(\lambda^2 - 0{\cdot}0689);\ \lambda_0 = 2630\ \text{A.}$$

TABLE XI.

*Rotatory Powers of α-Phenyl-γ-methylallyl Alcohol* (t, 20°; l, 0·5).

| | | | |
|---|---|---|---|
| $\lambda$ | 5780 | 5461 | 4358 |
| $\alpha_{obs.}$ | −29·16° | −33·59° | −64·0° |
| $\alpha_{calc.}$ | −29·20° | −33·70° | −63·8° |
| $\alpha_{obs.} - \alpha_{calc.}$ | − 0·04° | − 0·11° | + 0·2° |

and the dispersion ratio is insensitive to changes of temperature:

| | | | | | |
|---|---|---|---|---|---|
| $t$ | 20° | 36° | 40·5° | 62·5° | 71° |
| $\alpha_{4358}/\alpha_{5461}$ | 1·905 | 1·883 | 1·89 | 1·91 | 1·92 |

No data for its solutions are available, since this alcohol undergoes isomeric change into (II) somewhat readily.

It thus appears that the phenylalkylallyl alcohols exhibit simple rotatory dispersions. The values of $\lambda_0$ derived from the equations of Tables IX, X, and XI are respectively 2960, 2730, and 2630 A., and the tentative suggestion may be made that a large proportion of the rotatory power is due to induced dissymmetry of the phenyl group, since Baly and Tryhorn (J., 1915, **107**, 1058) found that a large number of benzene derivatives gave absorption bands in the region 2600—2750 A., and Kuhn (*Trans. Faraday Soc.*, 1930, **26**, 307) attributed a large induced dissymmetry to the benzene nucleus in mandelic acid.

Marked mutarotation was observed in alcohol (I), but alcohols (II), (IV), and (V) do not undergo mutarotation, whence it appears that this property may be associated with the symmetrical substitution in $\alpha\gamma$-dimethylallyl alcohol. The dispersion ratios at room temperature of the hydrogen phthalic and acetic esters of the various unsaturated alcohols in different solvents are recorded in Table XII.

TABLE XII.

*Values of the Dispersion Ratio,* $\alpha_{4358}/\alpha_{5461}$, *for Derivatives of Alcohols* (I)—(V).

| Derivative. | Solvent. | (I). | (II). | (III). | (IV). | (V). |
|---|---|---|---|---|---|---|
| Acetate .............................. | None | 1·79 | 1·93 | 3·00 | 2·00 | 1·75 |
| Hydrogen phthalate ............ | $Et_2O$ | 2·01 | — | 2·10 | — | — |
| ,, ,, ............ | $C_6H_6$ | 2·11 | 1·53 | — | 1·94 | 2·40 |
| ,, ,, ............ | $CHCl_3$ | 2·06 | 2·41 | — | 1·86 | 2·75 |
| ,, ,, ............ | $CS_2$ | 1·44 | — | — | 1·95 | 1·91 |
| ,, ,, ............ | $COMe_2$ | 1·99 | 1·77 | — | — | — |
| ,, ,, ............ | $C_2H_4Br_2$ | 2·06 | — | — | — | — |
| ,, ,, ............ | EtOH | 2·01 | — | — | 1·90 | 2·03 |
| ,, ,, ............ | $CCl_4$ | 2·27 | — | — | — | — |
| ,, ,, ............ | NaOH (aq.) | 1·98 | — | — | — | — |

Since the carboxylic esters of saturated aliphatic secondary alcohols exhibit complex rotatory dispersion, those derived from unsaturated alcohols are unlikely to be less complex. The dispersion ratios are in general greater than the value 1·65 associated with saturated aliphatic compounds and approximate to 2.

## EXPERIMENTAL.

*dl-n*-Propylpropenylcarbinol (b. p. 63—64·5°/14 mm., $n_D^{18^\circ}$ 1·4380) was prepared in 74% yield by the interaction of crotonaldehyde (0·9 mol.) and *n*-propylmagnesium chloride.

*dl-n*-Propylpropenylcarbinyl hydrogen phthalate was prepared by heating the *dl*-alcohol (137 g.) with phthalic anhydride (178 g.) and pyridine (95 g.) at 60—65° for 2 hours. The resultant oil, diluted with acetone, was poured into dilute hydrochloric acid and ice; the acid ester then separated as a solid, m. p. 58—62° (yield, almost theoretical). Purified through its sodium salt and crystallised from carbon disulphide, it formed prisms, m. p. 72·5° (Found, by titration with NaOH: *M*, 260. Calc. for $C_{15}H_{18}O_4$: *M*, 262).

(+)n-*Propylpropenylcarbinyl Hydrogen Phthalate.*—Strychnine (625 g.) was dissolved in a solution of the *dl*-hydrogen phthalic ester (491 g.) in dry chloroform; the solvent was removed, and hot dry acetone (1200 c.c.) added. On cooling, the strychnine salt (800 g.) separated. This was thrice recrystallised by solution in the minimum amount of methyl alcohol and addition of acetone. Further recrystallisation did not increase the optical activity of the salt, which was decomposed to yield a dextrorotatory hydrogen phthalic ester having $[\alpha]_{5461}$ + 19·3° in ethyl alcohol. The strychnine salt was readily decomposed by prolonged boiling in acetone solution, and by traces of water in the solvents, and could not be obtained optically pure. After repeated crystallisation from ether–light petroleum (+)n-*propylpropenylcarbinyl hydrogen phthalate* formed needles, m. p. 74°—75°, and attained the constant rotatory power $[\alpha]_{5461}^{18^\circ}$ + 22·85° (*l*, 2·0; *c*, 4·55) in ethyl-alcoholic solution (Found: C, 68·85; H, 6·9. $C_{15}H_{18}O_4$ requires C, 68·7; H, 6·9%).

Decomposition of the more soluble fractions of the strychnine salt yielded a hydrogen phthalic ester with $[\alpha]_{5461}$ − 9·5° in ethyl-alcoholic solution. By four recrystallisations of its brucine salt from acetone the rotatory power of this hydrogen phthalic ester was raised to a constant value of $[\alpha]_{5461}$ − 16·0° in ethyl-alcoholic solution. Finally, by repeated crystallisation

from ether and light petroleum, optically pure (−)*n*-propylpropenylcarbinyl hydrogen phthalate was obtained in needles, m. p. 75°, $[\alpha]_{5461}$ − 22·5° (*l*, 2·0; *c*, 4·610) in ethyl-alcoholic solution, and $[\alpha]_{5461}^{14.5°}$ + 17·2° (*l*, 2·0; *c*, 4·60) in carbon disulphide. In view of the failure of both the strychnine and the brucine salts to effect a complete resolution of this hydrogen phthalic ester, its salts with quinidine and cinchonidine were recrystallised from methyl acetate and acetone respectively: these, however, brought about little, if any, separation.

(+)n-*Propylpropenylcarbinol.*—Steam was passed through a solution of the (+) hydrogen phthalic ester (20 g.) and sodium hydroxide (7 g.) in water (34 c.c.) and from the steam-distillate (+)*n*-propylpropenylcarbinol, b. p. 63·5°/15 mm., $n_D^{18°}$ 1·4381, $d_{4°}^{19°}$ 0·839, was obtained. Its rotatory power is recorded in Table I, and the variations with solvent and temperature in Tables II and III. The carbinol (1·1 g.) was reconverted into its hydrogen phthalic ester, which had $[\alpha]_{5461}^{22°}$ + 21·1° (*l*, 2·0; *c*, 4·855), indicating slight racemisation during hydrolysis.

*Reduction of* (+)n-*Propylpropenylcarbinol to Di*-n-*propylcarbinol.*—The (+) alcohol ($\alpha_{5461}^{19°}$ + 4·02°, *l*, 0·5; 2 g.), dissolved in ethyl alcohol (99%; 15 c.c.), was reduced with hydrogen at 2 atms. in the presence of Raney nickel catalyst. The filtered solution was optically inactive to light of $\lambda_{5461}$ (*l*, 2·0), and yielded optically inactive di-*n*-propylcarbinol, b. p. 66·5°/18 mm., $n_D^{20°}$ 1·4216, which was converted into its hydrogen phthalic ester, m. p. 60° alone and when mixed with authentic di-*n*-propylcarbinyl hydrogen phthalate.

*Absence of Mutarotation in* (+)n-*Propylpropenylcarbinol.*—The (+) alcohol ($\alpha_{5461}^{19°}$ + 4·11°, $\alpha_{4359}^{19°}$ + 7·70°, *l*, 0·5) was maintained at 34—39° during 15 days; it was then kept at 20° for 6 hours, and the rotatory power redetermined, $\alpha_{5461}^{20°}$ + 4·10°, $\alpha_{4358}^{20°}$ + 7·95° (*l*, 0·5).

dl-n-*Propylpropenylcarbinyl acetate*, prepared by heating the *dl*-alcohol (6 g.) with acetic anhydride (8 g.) and pyridine (6 g.), had b. p. 63—64·5°/12 mm., $n_D^{17°}$ 1·4283 (Found: C, 69·2; H, 10·3. $C_8H_{14}O_2$ requires C, 69·2; H, 10·3%). (−)*n*-Propylpropenylcarbinyl acetate, prepared similarly from the (+) alcohol ($\alpha_{5461}^{19°}$ + 4·02°, *l*, 0·5), had b. p. 74°/16 mm., $n_D^{17°}$ 1·4270, $d_{4°}^{21°}$ 0·8815, $\alpha_{6438}^{21°}$ − 14·96°, $\alpha_{5893}^{21°}$ − 18·41°, $\alpha_{5780}^{21°}$ − 19·23°, $\alpha_{5461}^{21°}$ − 21·98°, $\alpha_{5086}^{21°}$ − 26·15°, $\alpha_{4800}^{21°}$ − 30·18°, $\alpha_{4678}^{21°}$ − 32·00°, $\alpha_{4359}^{21°}$ −38·40° (*l*, 0·5).

*Reduction of the* (−) *acetate.* The (−) acetate ($\alpha_{5461}^{21°}$ − 21·98°, *l*, 0·5; 3·6 g.) was reduced in ethereal solution by hydrogen at 2 atms. in the presence of platinum oxide. The filtered solution was inactive to light of $\lambda_{5461}$, and yielded optically inactive di-*n*-propylcarbinyl acetate, b. p. 69—70°/17 mm., $n_D^{19°}$ 1·4105.

dl-n-*Propylpropenylcarbinyl benzoate*, prepared by mixing the *dl*-alcohol (5·5 g.) with pyridine (5 g.) and adding benzoyl chloride (8·75 g.), had b. p. 146°/12 mm., $n_D^{14°}$ 1·5071 (Found: C, 76·7; H, 8·4. $C_{14}H_{18}O_2$ requires C, 76·9; H, 8·3%).

(+)*n*-Propylpropenylcarbinyl benzoate, prepared similarly from the (+) alcohol ($\alpha_{5461}^{18°}$ + 4·45°; *l*, 0·5), had b. p. 158°/16 mm., $d_{4°}^{18.5°}$ 0·9908, $n_D^{20°}$ 1·5046; its rotatory powers are recorded in Table V.

*Reduction of the* (+) *benzoate.* The (+) benzoate ($\alpha_{5461}^{20°}$ + 11·16°, *l*, 0·5; 3·1 g.) was reduced in ethereal solution (20 c.c.) by hydrogen at 2 atms. in the presence of platinum oxide; the filtered solution had $\alpha_{5461}^{18°}$ − 0·12° (*l*, 2·0), and from it optically inactive di-*n*-propylcarbinyl benzoate, b. p. 148—150°/11 mm., $n_D^{20°}$ 1·4883, was obtained.

dl-n-*Propylpropenylcarbinyl Methyl Ether.*—Methyl iodide (8 g.) was added to the potassium derivative obtained by the interaction of potassium (2 g.) and the *dl*-alcohol (5·7 g.) in benzene suspension; the crude methyl ether was freed from unreacted alcohol by heating with phthalic anhydride (6·5 g.) and pyridine (3·5 g.) for 2 hours at 65—70°. After redistillation through a short column, dl-n-*propylpropenylcarbinyl methyl ether* had b. p. 135°/760 mm., $n_D^{20.9°}$ 1·416, $d_{4°}^{20.5°}$ 0·7902 (Found: C, 75·0; H, 12·8. $C_8H_{16}O$ requires C, 74·9; H, 12·6%).

(+)*n*-Propylpropenylcarbinyl methyl ether was similarly prepared from the (−) alcohol ($\alpha_{5461}^{20°}$ − 2·14°; *l*, 0·5); it had b. p. 135—137°, $n_D^{20.8°}$ 1·4169, $\alpha_{6438}^{25.5°}$ + 3·73°, $\alpha_{5893}^{25.5°}$ + 4·53°, $\alpha_{5780}^{25.5°}$ + 5·03°, $\alpha_{5461}^{25.5°}$ + 5·50°, $\alpha_{5086}^{25.5°}$ + 6·21°, $\alpha_{4800}^{25.5°}$ + 7·04°, $\alpha_{4678}^{25.5°}$ + 7·38°, $\alpha_{4358}^{25.5°}$ + 9·01° (*l*, 0·2356).

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# 64. *Prototropy in Relation to the Exchange of Hydrogen Isotopes. Part IV. Isomerisation and Exchange in Methyleneazomethines.*

By EDUARDO DE SALAS and CHRISTOPHER L. WILSON.

Measurements are recorded of the rates of isomerisation and isotopic hydrogen exchange of the following pair of tautomerides under uniform conditions:

$$p\text{-MeO}\cdot C_6H_4\cdot CH_2\cdot N{:}CHPh \rightleftharpoons p\text{-MeO}\cdot C_6H_4\cdot CH{:}N\cdot CH_2Ph$$

Previous evidence is reviewed which shows that the interconversion of these structures proceeds by the simultaneous abstraction and addition of a proton. On this basis each act of isomerisation will lead to exchange. However, the experimental results show that exchange, at least for one isomer and possibly for both, occurs faster than isomerisation. It is therefore suggested that an additional mechanism of exchange exists which involves the direct replacement of the mobile hydrogen by deuterium without isomerisation. The stereochemical course of this superimposed exchange reaction is considered.

IN some investigations closely related to those of the present series, it was shown that tautomerism *in the methyleneazomethine system (I $\rightleftharpoons$ II) involves the simultaneous* rather than the consecutive withdrawal and addition of a proton (Hsü, Ingold, and Wilson, J., 1935, 1778):

$$\text{(I.)} \quad R^1R^2CH\cdot N{:}CR^3R^4 \rightleftharpoons R^1R^2C{:}N\cdot CHR^3R^4 \quad \text{(II.)}$$

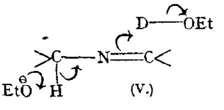
This followed from the observation that, independently of the nature of $R^1 \ldots R^4$, the racemisation of an isomeride could be quantitatively accounted for by the cycle: active (I) ⟶ inactive (II) ⟶ inactive (I); for, had the proton transfers been consecutive, the rate of racemisation should have been augmented by the cycle: active (I) ⟶ inactive anion ⟶ *inactive (I); whereas no such increase of rate was observed.*

We have now studied the isotopic hydrogen exchange of a pair of tautomeric methyleneazomethines. This paper describes measurements of the rate with which each isomer of the system (III $\rightleftharpoons$ IV) exchanges its protium for deuterium of the solvent, ethyl alcohol, together with a determination of the velocity of interconversion of the isomerides under the same conditions. The tautomerism of these compounds

$$\text{(III.)} \quad p\text{-MeO}\cdot C_6H_4\cdot CH_2\cdot N{:}CHPh \rightleftharpoons p\text{-MeO}\cdot C_6H_4\cdot CH{:}N\cdot CH_2Ph \quad \text{(IV.)}$$

in alcoholic solution with catalysis by ethoxide ions has already been investigated (Ingold and Shoppee, J., 1929, 1199). In the present work, each compound was allowed to isomerise for various times in alcohol containing a known proportion of deuterium ethoxide and the sodium ethoxide catalyst, and the isolated mixtures of azomethines were analysed both for isomeric composition and for deuterium content.

It is evident [see formula (V)] that if the interconversion of the compounds (III) and (IV) conforms to the suggested mechanism of simultaneous transfers, each act of isomerisation will lead to hydrogen exchange, *i.e.*, the replacement of original protons by either new protons or deuterons. The rate of hydrogen exchange must, therefore, be at least equal to that of the tautomerism: it may, however, be the larger, if, besides the isomerisation, any other mechanism of exchange exists not involving tautomerism.



(V.)

The results are in the table, but before considering the rates, it may be noted that each molecule has three hydrogen atoms which would be expected to undergo replacement. The fact that three are indeed replaced is supported by the data obtained in the experiments run for long times: the exchange numbers are 1·9—2·0, and if the number of atoms replaceable is 3, then the average equilibrium constant for the separate exchanges must be 2·0/3 ∼ 0·7, a value quite close to that expected from known vibration frequencies.

Owing to the reversibility of isomerisation and to the three successive stages of exchange, it is convenient to consider initial rates: these involve only the forward reaction and exchange with respect to only one position. Even so, the results can be treated only qualitatively, since we do not know the relative rates of transference of protium and deuterium in the forward reaction of either isomeride. If we were able to assume these rates to be the same, then the figures termed "Isomerisation %" in the table would be

*Isomerisation and Deuterium Exchange of the Methyleneazomethines* (III) *and* (IV) *in Deuterium Ethoxide catalysed by Ethoxide Ions.*

| D content of solvent, 100[EtOD]/([EtOD] + [EtOH]) | | 31·5. | | | | 94·4. | |
|---|---|---|---|---|---|---|---|
| Compound (III) used | Time (hrs.) | 4·0 | 8·0 | 984 | — | 0·5 | 1·0 |
| | Isomerisation (IV %) | 21·0 | 39·0 | — | — | 15·0 | 22·5 |
| | Combustion water: excess *d* (p.p.m.) | 322 | 541 | 4316 | — | 493 | 987 |
| | Combustion water: D, atoms % | 0·299 | 0·504 | 4·02 | — | 0·459 | 0·919 |
| | D (atoms %) in one position * | 4·48 | 7·56 | 60·3 | — | 6·89 | 13·79 |
| | Exchange (%) † | 14·3 | 24·0 | 191·4 | — | 7·3 | 14·6 |
| Compound (IV) used | Time (hrs.) | 4·0 | 8·0 | 24·0 | 744 | 0·5 | 1·0 |
| | Isomerisation (III %) | 6·5 | 12·3 | 23·4 | — | 4·2 | 7·8 |
| | Combustion water: excess *d* (p.p.m.) | 329 | 605 | 1344 | 4502 | 422 | 900 |
| | Combustion water: D, atoms % | 0·306 | 0·563 | 1·25 | 4·19 | 0·393 | 0·838 |
| | D (atoms %) in one position * | 4·59 | 8·45 | 18·8 | 62·8 | 5·40 | 12·57 |
| | Exchange (%) † | 14·6 | 26·8 | 59·6 | 199·4 | 5·7 | 13·3 |

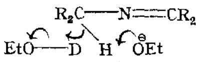
* These figures are obtained from those of the previous line by multiplication by 15, the number of hydrogen atoms in the compounds burnt.

† These are percentage expressions of so-called exchange numbers, *i.e.*, the average number of atoms per molecule exchanged, calculated as if one atom in each molecule is exchangeable and as if deuterons and protons are always transferred at the same specific rate. The slight fall in isotopic composition of the solvent during a run is disregarded.

directly comparable with those labelled "Exchange %". Inasmuch as protons have always been found to be transferred more rapidly than deuterons in the same reaction, the real percentages of exchange are probably greater than the tabulated figures, and the excess of the real over these "apparent" percentages is likely to be greater in the more dilute deuterium solvent, where the competition of the more mobile protons is relatively more serious.

Viewing the initial rates in this light, we can conclude that, at least in the example of compound (IV), and possibly also in its isomeride (III), the rate of exchange is greater than can be accounted for by isomerisation alone.

This suggests an additional exchange mechanism and one naturally postulates simultaneous proton transfers at the same carbon atom as illustrated in (VI). Again nc quantitative conclusions can be drawn, because we do not know the relation of the twc component rates (introduction of H and D) of this extra reaction to those of the exchang dependent on isomerisation, or how this unknown relation is modified by a change of sol vent. We can say, however, that whatever the mechanism c the additional reaction may be, it cannot lead to racemisatio (which goes no faster than isomerisation) so that if indeed : has the form shown in (VI) the stereochemical configuration c the carbon atom attacked must remain unaltered by the sul stitution. It should perhaps be explained that, as stated by Hsü, Ingold, and Wilson (*lo cit.*), we do not regard the proton transfers as quite simultaneous: the organic ion considered to be partly liberated, but not completely enough, or for long enough, to chan its stereochemical form. On account of this conclusion we have put in hand several seri of experiments, designed directly to test this stereochemical course of the substituti of hydrogen for hydrogen by the various recognised mechanisms.




(VI.)

## Experimental.

*Benzylidene*-p-*methoxybenzylamine* (III) *and* p-*Methoxybenzylidenebenzylamine* (IV).—T azomethines were prepared by Ingold and Shoppee's method (*loc. cit.*); (III) was purif

by distillation, b. p. 170°/0·2 mm. (yield 64%); and (IV) by recrystallisation from petrol (b. p. 40—60°), then having m. p. 42—43° (yield 71%).

*Analysis of Mixtures of the Azomethines.*—A modification of the method described by Shoppee (J., 1931, 1232) was used. Twice the theoretical amount of *p*-nitrophenylhydrazine was dissolved in concentrated hydrochloric acid (2 c.c.), the solution diluted to 20 c.c. with water, and filtered at about 60° into a mixture of the azomethines and water (50 c.c.). The resulting liquid was shaken for 3 hours and the precipitated hydrazones were filtered off, washed with dilute hydrochloric acid and water until free from excess of the hydrazine, dried, and weighed (yield, quantitative), and their m. p.'s determined.

The composition of the mixture was obtained by reference to a graph of the figures obtained from mixtures of the *p*-nitrophenylhydrazones prepared in the above manner from artificial mixtures of the azomethines. It is estimated that the isomerisation figures in the table are accurate to $\pm$ 1·0%.

*Preparation of Deuterium Ethoxide Solutions.*—A solvent containing 31·5 mols. % of deuterium ethoxide was prepared according to Ingold, de Salas, and Wilson (J., 1936, 1333). Hydrolysis of ethyl sulphite by a little more than the equivalent amount of deuterium oxide gave a product which, dried by freshly ignited lime and magnesium amalgam, had $d_{4^\circ}^{25^\circ}$ 0·8033 and contained 94·4 mols. % of deuterium ethoxide.

*Isomerisation of the Azomethines in Deuterium Ethoxide.*—The appropriate azomethine (*x* g.) was dissolved in 0·1N-sodium ethoxide (2·5*x* c.c.) prepared in the deuterium ethoxide. The solutions were heated for various times in sealed bulbs to 74·0°. Reaction was arrested by cooling and breaking the bulbs under water; the azomethines were then extracted with ether. The ethereal solution was well washed with distilled water to remove alcohol, dried, and evaporated. The residual azomethine mixture was thoroughly dried in a vacuum over phosphoric oxide. A portion of the mixture was treated with *p*-nitrophenylhydrazine as already described, and the remainder was analysed for deuterium by the customary method involving combustion and density determination of the water so produced. The results are in the table.

The authors thank Professor C. K. Ingold, D.Sc., F.R.S., for his help in this work.

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## 65. *The Unsaturation and Tautomeric Mobility of Heterocyclic Compounds. Part XI. α- and β-Naphthoxazole and 5-Bromobenzoxazole Derivatives. The Ultra-violet Absorption Spectra of Some Tautomeric Selenazoles.*

By R. D. DESAI, R. F. HUNTER, and A. RAHMAN KHAN KHALIDI.

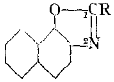
The α- and β-naphthoxazoles containing prototropic triad systems exhibit a close analogy to their thiazole analogues in their behaviour towards methylating agents. 1-Amino-α-naphthoxazole and its β-analogue react exclusively in the amino-aromatic form with methyl iodide, yielding iminomethyldihydro-derivatives. The phenyl group in anilinonaphthoxazoles, however, enables the nitrogen atom to which it is attached to compete with the ring nitrogen atom during methylation. The hydroxy- and thiolnaphthoxazoles also resemble their benzoxazole analogues on methylation under the usual conditions.

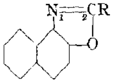
The orientation of the 5-bromo-derivatives obtained by bromination of 1-hydroxybenzoxazole and 1-thiolbenzoxazole follows from their rational syntheses, and their methylation gives rise to the expected *N*- and *S*-methyl derivatives.

The ultra-violet absorption spectrum of 1-hydroxybenzselenazole in methyl alcohol is almost identical with that of the *N*-methyl ether, showing that the covalent form of the molecule has the ketodihydro-structure. In aqueous sodium hydroxide, however, there is a drop in the first maximum between 2800 and 2900 A., and a shift of the curve towards the region of longer wave-length. The curve of 1-thiolbenzselenazole in methyl alcohol also indicates that this molecule has the thiodihydro-structure. In aqueous

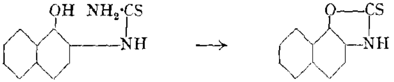
sodium hydroxide, there is a slight shift towards the region of shorter wave-length, and an appreciable drop in the first maximum connected with the ionisation of the hydrogen atom of the triad system.

As might be anticipated on the basis of the theory of sextuple valency group stability, α- and β-naphthoxazoles (I and II) containing prototropic triad systems exhibit a striking similarity to their thiazole analogues in their behaviour towards alkylating agents (compare Desai, Hunter, and Khalidi, J., 1934, 1186).

(I.) 

 (II.)

1-*Amino-α-naphthoxazole* (I, R = $NH_2$) was synthesised from 1-*hydroxy*-2-*naphthylthiourea* by treatment with freshly precipitated mercuric oxide in alcohol, but in somewhat poor yield, as the greater portion of the material underwent oxazole ring formation of quite a different type, leading to the production of 1-thiol-α-naphthoxazole. Since there is every reason to suppose that thioureas possess the thioamide structure in the covalent form (Hendrick, *J. Amer. Chem. Soc.*, 1928, **50**, 2455; compare Hunter and Jones, J., 1930, 2194), this reaction is readily explicable on the view that the proximity of the hydroxyl and the amino-group permits facile elimination of ammonia with the production of the thiolnaphthoxazole:



On methylation with methyl iodide, 1-amino-α-naphthoxazole reacted apparently exclusively in the amino-aromatic form (III, X = NH), yielding 1-*imino*-2-*methyl*-1 : 2-*dihydro-α-naphthoxazole* (V, R = H), unaccompanied by any detectable amount of 1-*methylamino-α-naphthoxazole* (VI, R = H) (compare Hunter and Jones, J., 1930, 941), which was synthesised for comparison from 1-thiol-α-naphthoxazole and methylamine.

(III.) $C_{10}H_6{<}^{O}_{N}{>}C{\cdot}X[H]$ ⇌ $C_{10}H_6{<}^{O}_{N[H]}{>}C{:}X$ (IV.)

(V.) $C_{10}H_6{<}^{O}_{NMe}{>}C{:}NR$ $C_{10}H_6{<}^{O}_{N}{>}C{\cdot}NMeR$ (VI.)

The phenyl group of the anilino-substituent in 1-anilino-α-naphthoxazole (III ⇌ IV, X = NPh), however, enables the nitrogen atom to which it is attached to compete with the ring nitrogen atom during methylation, leading to the production of 1-*phenylmethylamino-α-naphthoxazole* (VI, R = Ph) in substantial amount alongside the 1-*phenylimino*-2-*methyl*-1 : 2-*dihydro*-isomer (V, R = Ph) which constitutes the bulk of the methylation product. This result falls into line with the behaviour of the corresponding thiazole derivative, since a repetition of the methylation of 1-anilino-α-naphthathiazole (Chowdhury, Desai, and Hunter, *J. Indian Chem. Soc.*, 1933, **10**, 637) has shown that 1-phenylmethylamino-α-naphthathiazole is produced to the extent of about 12% (unpublished results).

1-*Hydroxy-α-naphthoxazole* was synthesised by condensation of ethyl chloroformate and 2-amino-1-naphthol. It was also prepared by the action of carbonyl chloride on the aminonaphthol, and by condensation of the latter with urethane. On methylation in alkaline medium, it gave 1-*keto*-2-*methyl*-1 : 2-*dihydro-α-naphthoxazole* (V, with O in place of NR).

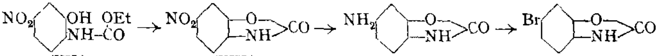
2-*Amino-β-naphthoxazole* (II, R = $NH_2$), synthesised from 2-*hydroxy*-1-*naphthylthiourea*, behaved similarly to the α-derivative and to its thiazole analogue (Desai, Hunter and Kureishy, J., 1936, 1668) and gave 2-*imino*-1-*methyl*-1 : 2-*dihydro-β-naphthoxazole*

on methylation. 2-Anilino-β-naphthoxazole gave rise to a mixture of 2-*phenylimino*-1-*methyl*-1 : 2-*dihydro*-β-*naphthoxazole* and 2-*phenylmethylamino*-β-*naphthoxazole* on methylation, in which the former predominated to the extent of about 75%.

2-*Hydroxy*-β-*naphthoxazole*, which was synthesised from 1-amino-2-naphthol by all three methods, underwent methylation on the nuclear nitrogen atom under the usual conditions.

On methylation with methyl iodide in methyl-alcoholic sodium methoxide solution and also on treatment with methyl sulphate in the presence of aqueous potassium hydroxide, 2-thiol-β-naphthoxazole gave solely the S-*methyl* ether. No evidence was obtained of the presence of 2-*thio*-1-*methyl*-1 : 2-*dihydro*-β-*naphthoxazole*, which was synthesised from 2-keto-1-methyl-1 : 2-dihydro-β-naphthoxazole and phosphorus pentasulphide.

The constitution of the bromo-substitution derivative previously obtained from 1-hydroxybenzoxazole (Desai, Hunter, and Khalidi, *loc. cit.*) has now been established by its identity with 5-*bromo*-1-*hydroxybenzoxazole* (X), synthesised from 5-nitro-2-aminophenol by cyclisation of the *ester* (VII), reduction of the 5-*nitro*-derivative (VIII), and replacement of the amino-group in the *base* (IX) by bromine.



(VII.) (VIII.) (IX.) (X.)

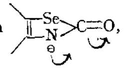
As might be anticipated, methylation of 5-bromo-1-hydroxybenzoxazole in alkaline medium gave the N-*methyl* ether, whose constitution follows from its preparation by bromination of 1-keto-2-methyl-1 : 2-dihydrobenzoxazole (compare Hunter, J., 1930, 125).

The orientation of the bromo-substitution derivative of 1-thiolbenzoxazole as the 5-*bromo*-derivative was accomplished by a similar synthesis from 5-*nitro*-1-*thiolbenzoxazole*, obtained from 5-nitro-2-aminophenol and carbon disulphide. The methylation of 5-bromo-1-thiolbenzoxazole gave the expected S-*methyl* ether, which was also obtained by direct bromination of 1-methylthiolbenzoxazole. No evidence of the formation of an isomeric methyl ether was obtained (compare Chiragh Hasan and Hunter, J., 1936, 1672).

### *The Absorption Spectra of Selenazole Derivatives.*

An examination of the ultra-violet absorption spectra of the selenazoles previously studied (Chiragh Hasan and Hunter, J., 1935, 1766) affords interesting confirmation of their striking similarity to thiazole analogues. For instance, the curve of 1-hydroxybenzselenazole (XI ⇌ XII) in methyl alcohol is almost identical with that of 1-keto-2-methyl-1 : 2-dihydrobenzselenazole (Fig. 1), showing that the covalent form of the molecule has the ketodihydro-structure (XII).

$$\text{(XI.)} \quad C_6H_4{<}{\substack{Se\\N}}{\gg}C{\cdot}OH \quad \rightleftharpoons \quad C_6H_4{<}{\substack{Se\\NH}}{>}CO \quad \text{(XII.)}$$

The drop in the first maximum of the hydroxybenzselenazole between 2800 and 2900 A., which is characteristic of the carbonyl group, in aqueous sodium hydroxide may be attributed to the decrease in concentration of absorbing molecules consequent on the production of the ion  in which some distribution of the negative charge in the sense of the arrows would be anticipated. The shift of the curve towards the region of longer wave-length also indicates deformation of the type observed in the case of 1-hydroxy-5-methylbenzthiazole (Hunter and Parken, J., 1935, 1755).

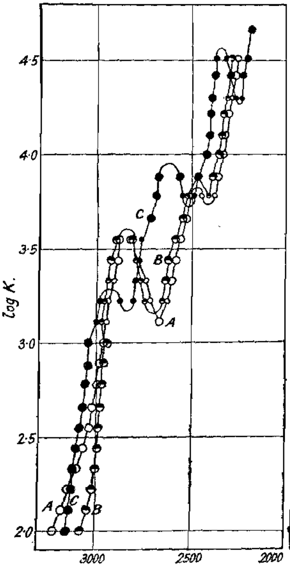
The curve of 1-thiolbenzselenazole (XI ⇌ XII, with S in place of O) was almost identical with that of 1-thio-2-methyl-1 : 2-dihydrobenzselenazole (Fig. 2) (compare Chiragh Hasan and Hunter, J., 1936, 1672).

In aqueous sodium hydroxide solution, 1-thiolbenzselenazole gave a curve belonging to the same family, but slightly shifted towards the region of shorter wave-length, and

hibiting an appreciable drop in the first maximum due to ionisation of the hydrogen om of the triad system.

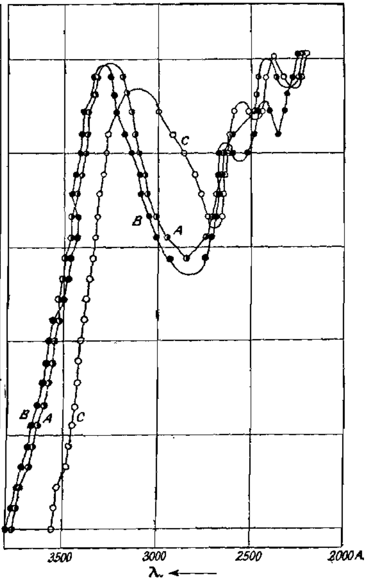
Both in the thiazoles and in the selenazoles, the shift in absorption curves of the

FIG. 1.




A = 1-*Hydroxybenzselenazole in* MeOH.
B = 1-*Keto-2-methyl-1 : 2-dihydrobenzselenazole in* MeOH.
C = 1-*Hydroxybenzselenazole in* NaOH.

FIG. 2.




A = 1-*Thiolbenzselenazole in* MeOH.
B = 1-*Thio-2-methyl-1 : 2-dihydrobenzselenazole in* MeOH.
C = 1-*Thiolbenzselenazole in* NaOH.

1-hydroxy- and 1-thiol derivatives due to deformation in aqueous sodium hydroxide takes place in opposite directions.

## EXPERIMENTAL.

The method of reducing 2-nitro-1-naphthol (Hodgson and Kilner, J., 1924, **125**, 807) to 2-amino-1-naphthol recommended by Fischer and Hamer (J., 1934, 963) proved unsatisfactory in our hands, and the following procedure was therefore adopted. A solution of 2-nitro-1-naphthol (10 g.) in slightly more than its equivalent of dilute aqueous sodium hydroxide (4 g. in 300 c.c. of water) was heated to boiling and the filtered solution was treated with sodium hyposulphite (50 g.) until the red colour disappeared; the aminophenol separated, on cooling, as a mass of colourless crystals, m. p. 150° (darkening at 130°). Since this compound is more stable in the form of its hydrochloride, the aminonaphthol was dissolved in warm 10% hydrochloric acid (250 c.c.), and the filtered solution was mixed with hydrochloric acid (150 c.c.) and kept, the hydrochloride separating in almost quantitative yield, m. p. 260°.

1-*Hydroxy-2-naphthylthiourea*.—A solution of the hydrochloride of the aminonaphthol (10 g.), potassium thiocyanate (10 g.), and concentrated hydrochloric acid (20 c.c.) in water

(100 c.c.) was heated on a water-bath for 10 hours. The residue obtained after removal of inorganic salts by extraction with hot water, and treatment with ethyl acetate, was recrystallised from alcohol, the *thiourea* being obtained in small needles (10 g.), m. p. 252° (Found: S, 14·7. $C_{11}H_{10}ON_2S$ requires S, 14·6%). This thiourea is very sensitive to air and turns black on keeping, although the m. p. remains unaffected.

*1-Amino-α-naphthoxazole.*—When a solution of 1-hydroxy-2-naphthylthiourea (10 g.) in alcohol (100 c.c.) was heated under reflux with freshly precipitated mercuric oxide (25 g.) for 18—20 hours, ammonia was evolved. The filtrate, after removal of mercuric sulphide, was evaporated to dryness, and the residue treated with 10% aqueous sodium hydroxide. The alkali-insoluble residue, when warmed with benzene, partly dissolved, yielding a solution which on filtration and concentration deposited the *aminonaphthoxazole* (1·5—2 g.) in needles, m. p. 195° after recrystallisation from alcohol (Found: C, 71·7; H, 4·25. $C_{11}H_8ON_2$ requires C, 71·7; H, 4·3%). The *acetyl* derivative, prepared by heating a solution of the base in acetic anhydride, separated from dilute alcohol in needles, m. p. 210° (Found: C, 69·1; H, 4·3. $C_{13}H_{10}O_2N_2$ requires C, 69·0; H, 4·4%).

The residue insoluble in benzene consisted of the mercury salt of 1-thiol-α-naphthoxazole, which decomposed at about 300°. The alkaline extract on acidification gave a precipitate which on recrystallisation furnished 1-thiol-α-naphthoxazole (3·5 g.), m. p. and mixed m. p. 262°.

*Methylation.*—A mixture of 1-amino-α-naphthoxazole (1·5 g.) and methyl iodide (3·2 c.c.) was heated in a sealed tube at 100° for 16 hours; the product was basified and extracted with chloroform. The sticky residue obtained by removal of chloroform was treated with methyl alcohol (5 c.c.), and the residue recrystallised from alcohol; *1-imino-2-methyl-1 : 2-dihydro-α-naphthoxazole* was obtained in small needles, m. p. 154° (Found: C, 72·8; H, 5·1. $C_{12}H_{10}ON_2$ requires C, 72·7; H, 5·05%). A mixture of this with the isomeric 1-methylamino-derivative had m. p. 140°. The *1-acetimido-2-methyl-1 : 2-dihydro*-derivative separated from dilute alcohol in needles, m. p. 133° (Found: C, 70·1; H, 5·0. $C_{14}H_{12}O_2N_2$ requires C, 70·0; H, 5·0%).

*Synthesis of 1-Methylamino-α-naphthoxazole.*—A mixture of 1-thiol-α-naphthoxazole (1 g.) and methylamine (4 c.c. of a 30% solution) was heated in a sealed tube at 100° for 12 hours, the product extracted with ether, and the extract washed with 10% aqueous sodium hydroxide. The residue obtained after removal of the ether was crystallised from dilute methyl alcohol; the *1-methylamino*-base separated in needles, m. p. 160° (Found: C, 72·7; H, 4·95. $C_{12}H_{10}ON_2$ requires C, 72·7; H, 5·05%). The *acetyl* derivative of this crystallised from dilute alcohol in needles, m. p. 136° (Found: C, 70·2; H, 5·0 $C_{14}H_{12}O_2N_2$ requires C, 70·0; H, 5·0%).

*1-Anilino-α-naphthoxazole.*—This was prepared by heating 1-thiol-α-naphthoxazole with aniline at 200° for 8 hours. The product was recrystallised from benzene and converted into picrate, and the base liberated by warm dilute alkali solution. After recrystallisation from alcohol or benzene, it had m. p. 236° (Found: C, 78·5; H, 4·65. Calc. for $C_{17}H_{12}ON_2$: C, 78·5; H, 4·6%). The picrate separated from benzene in small yellow needles, m. p. 218—220° (Found: C, 56·6; H, 3·0 Calc. for $C_{17}H_{12}ON_2,C_6H_3O_7N_3$: C, 56·4; H, 3·1%). Jacobson (*Ber.*, 1889, **22**, 3242) recorded m. p. 232—233° and 213—214°, respectively.

*Methylation.*—The base (2 g.) was heated with methyl iodide (3 c.c.) at 100° for 18 hours, and the product basified and extracted with chloroform. The gum obtained was dissolved in benzene and heated under reflux with a solution of picric acid (1·3 g.) in the same solvent for an hour. The residue obtained on evaporation of benzene was treated with ethyl acetate (10 c.c.); the filtered extract deposited the *picrate* of 1-phenylimino-2-methyl-1 : 2-dihydro-α-naphthoxazole in small yellow needles, m. p. 188° (Found: C, 57·3; H, 3·3. $C_{18}H_{14}ON_2,C_6H_3O_7N_3$ requires C, 57·25; H, 3·4%). This constituted about 75% of the product. Recrystallisation of the residue (from the ethyl acetate extract) from benzene furnished the *picrate* of 1-phenylmethylamino-α-naphthoxazole in yellow needles, m. p. 208° (Found: C, 57·0; H, 3·3%), which were identified by mixed m. p. determination with the specimen described below.

*Synthesis of 1-Phenylmethylamino-α-naphthoxazole.*—A mixture of 1-thiol-α-naphthoxazole (1 g.) and methylaniline (1 g.) was heated in an oil-bath at 180—190° for 8 hours. The product was extracted with dilute hydrochloric acid and with dilute aqueous sodium hydroxide, and a solution of the residual gum in benzene was treated with the calculated quantity of picric acid; the picrate of the 1-phenylmethylamino-base was obtained in needles, m. p. 207—208°.

*1-Hydroxy-α-naphthoxazole.*—(i) *Condensation of 2-amino-1-naphthol with ethyl chloroformate.* A solution of 2-amino-1-naphthol hydrochloride (3 g.) in ethyl-alcoholic sodium ethoxide (0·7 g. of sodium and 45 c.c. of absolute alcohol) was cooled in ice during the gradual addition of chloroformic ester (2 g.), and the mixture was heated under reflux for 6 hours. The gummy

residue obtained by removal of alcohol was heated in an oil-bath at 180—190° for 3 hours, and the cyclised product extracted with aqueous sodium hydroxide (10%). The 1-*hydroxy*-*α*-*naphthoxazole* recovered on acidification crystallised from alcohol in needles (2·2 g.), m. p. 218—220° (Found: C, 71·5; H, 3·8. $C_{11}H_7O_2N$ requires C, 71·35; H, 3·8%). The m. p. was not raised by further recrystallisation from benzene.

(ii) *Action of carbonyl chloride on* 2-*amino*-1-*naphthol.* A mixture of the hydrochloride of 2-amino-1-naphthol (2 g.), pyridine (30 c.c.), and a 12% solution of carbonyl chloride in toluene (10 c.c.) was vigorously shaken at intervals during 3 hours and thereafter kept for 24 hours. The residue obtained by removal of toluene and pyridine was extracted with 10% aqueous sodium hydroxide, and the hydroxynaphthoxazole (m. p. 208°) recovered by acidification. On recrystallisation from alcohol this was obtained in small needles, m. p. 220°, not depressed by the specimen already described. A residue, insoluble in hot aqueous alkali and in alcohol and acetone, crystallised from glacial acetic acid in black needles, m. p. 268°.

(iii) *Synthesis from* 2-*amino*-1-*naphthol and urethane.* An intimate mixture of the amino-naphthol (3·2 g.) and urethane (2 g.) was heated at 160° for 4 hours, ammonia being evolved. Extraction of the cooled melt with aqueous alkali furnished the hydroxynaphthoxazole, m. p. 220° after recrystallisation from alcohol and benzene.

*Methylation.* A solution of the hydroxy-derivative (1 g.) in warm chloroform was shaken with aqueous potassium hydroxide (33%, 10 c.c.) and methyl sulphate (6 c.c.). Destruction of the excess of methyl sulphate with alkali and extraction with chloroform gave 1-*keto*-2-*methyl*-1 : 2-*dihydro*-*α*-*naphthoxazole*, which crystallised from dilute alcohol in small needles, m. p. 198° (Found: C, 72·3; H, 4·6. $C_{12}H_9O_2N$ requires C, 72·3; H, 4·5%). Attempts to bring about hydrolytic ring fission by boiling the ketomethyldihydro-derivative with concentrated hydrochloric acid and also by heating with this acid in a sealed tube at 180° proved unsuccessful. The oxazole ring underwent fission, however, on treatment with 50% sulphuric acid at 160° for 12 hours.

1-Amino-2-naphthol was most conveniently prepared by reduction of Orange II in alkaline solution with sodium hyposulphite, and purified by conversion into its hydrochloride, which crystallised in long needles, m. p. 250—252°.

2-*Hydroxy*-1-*naphthylthiourea*, prepared as in the case of the 1-hydroxy-2-naphthyl derivative, formed small needles, decomp. about 300° (Found: S, 14·9. $C_{11}H_{10}ON_2S$ requires S, 14·7%), which turned black on exposure to air.

2-*Amino*-*β*-*naphthoxazole.*—A solution of 2-hydroxy-1-naphthylthiourea (10 g.) in alcohol (80 c.c.) was treated with freshly precipitated mercuric oxide (20—25 g.), and the mixture heated under reflux for 24—28 hours. The product obtained by evaporation of the filtered solution was treated with warm aqueous sodium hydroxide, and the residue extracted with warm benzene. 2-*Amino*-*β*-*naphthoxazole* separated in plates, m. p. 176° (Found: C, 71·9; H, 4·4. $C_{11}H_8ON_2$ requires C, 71·4; H, 4·4%). The benzene-insoluble residue consisted of the mercuric mercaptide, m. p. 276—278°. The *acetyl* derivative, obtained by acetylation of the amino-naphthoxazole with acetic anhydride, crystallised from dilute alcohol in small needles, m. p. 212° (Found: C, 69·2; H, 4·3. $C_{13}H_{10}O_2N_2$ requires C, 69·0; H, 4·4%).

The alkaline extract from the original crude product, on acidification, deposited 2-thiol-β-naphthoxazole, which was identified by m. p. and mixed m. p. determination.

*Methylation.* The product obtained by heating 2-amino-β-naphthoxazole (1·5 g.) with methy[l] iodide (3·2 c.c.) at 100° for 20 hours was basified and extracted with chloroform; 2-*imino*-1-*methyl*-1 : 2-*dihydro*-*β*-*naphthoxazole* was then obtained, which crystallised from dilute alcoh[ol] in small needles, m. p. 148—150° (Found: C, 72·7; H, 5·0 $C_{12}H_{10}ON_2$ requires C, 72·7; H, 5·05%). 2-*Acetimido*-1-*methyl*-1 : 2-*dihydro*-*β*-*naphthoxazole* crystallised from dilute alcoh[ol] in needles, m. p. 132° (Found: C, 70·1; H, 5·0. $C_{14}H_{12}O_2N_2$ requires C, 70·0; H, 5·0%).

2-*Methylamino*-*β*-*naphthoxazole*, prepared by heating 2-thiol-β-naphthoxazole with exce[ss] of aqueous methylamine (30%) at 100° for 14 hours, crystallised from dilute methyl alcohol i[n] long needles, m. p. 158° (Found: C, 72·8; H, 5·15. $C_{12}H_{10}ON_2$ requires C, 72·7; H, 5·05%[).] The *acetyl* derivative separated from dilute alcohol in needles, m. p. 140° (Found: C, 70·0[;] H, 5·0. $C_{14}H_{12}O_2N_2$ requires C, 70·0; H, 5·0%).

2-Anilino-β-naphthoxazole crystallised from dilute alcohol in small needles, m. p. 17[?] (Found: C, 78·6; H, 4·8. Calc. for $C_{17}H_{12}ON_2$: C, 78·5; H, 4·6%); the picrate form[ed] yellow needles, m. p. 210—212° (Found: C, 56·4; H, 3·15. Calc. for $C_{17}H_{12}ON_2,C_6H_3O_7N_3$: C, 56·4; H, 3·1%). Jacobson (*Ber.*, 1888, **21**, 417) recorded m. p. 167—168° and 207—20[8°] respectively.

*Methylation of* 2-*Anilino*-*β*-*naphthoxazole.*—The gum isolated by chloroform extraction of t[he]

product formed by the methylation of 2-anilino-β-naphthoxazole (2 g.) with methyl iodide (3·5 c.c.) at 100° for 24 hours was dissolved in acetone and converted into picrate. Crystallisation gave mixtures, and the product obtained by removal of acetone was therefore shaken with ethyl acetate. The filtrate deposited the *picrate* of 2-phenylimino-1-methyl-1 : 2-dihydro-β-naphthoxazole in small yellow needles, m. p. 174—176° (Found: C, 57·2; H, 3·4. $C_{18}H_{14}ON_2,C_6H_3O_7N_3$ requires C, 57·25; H, 3·4%). This constituted about 75% of the total picrate. The residue which was sparingly soluble in ethyl acetate crystallised from benzene in small yellow needles, m. p. 194—196°, and was identified as the *picrate* of 2-phenylmethylamino-β-naphthoxazole (Found: C, 57·4; H, 3·3%).

*Synthesis of 2-Phenylmethylamino-β-naphthoxazole.*—A mixture of 2-thiol-β-naphthoxazole (1 g.) and methylaniline (1 g.) was heated at 180° for 8 hours. The base was obtained as a gum; this furnished a picrate which crystallised in needles, m. p. 196°.

*2-Hydroxy-β-naphthoxazole.*—(i) *Condensation of 1-amino-2-naphthol with ethyl chloroformate.* The reaction was carried out as in the case of the α-naphthoxazole, the mixture being heated for 8 hours. The resinous product obtained by removal of alcohol was extracted with water and thereafter heated at 180—190° for 4 hours, and the *2-hydroxy-β-naphthoxazole* was extracted with aqueous alkali and recrystallised from dilute alcohol, forming small needles (2·4 g.), m. p. 208° (Found: C, 71·3; H, 3·7. $C_{11}H_7O_2N$ requires C, 71·4; H, 3·8%).

(ii) *Action of carbonyl chloride on 1-amino-2-naphthol.* The hydroxynaphthoxazole, m. p. 207—208°, was obtained in nearly 50% yield, accompanied by a substance, m. p. 250°, which was insoluble in aqueous alkali.

(iii) *Synthesis from 1-amino-2-naphthol and urethane.* An intimate mixture of the hydrochloride of the aminonaphthol (6 g.) and urethane (3 g.) was heated at 190° for 6 hours, and the hydroxynaphthoxazole (4·5 g., m. p. 280° after recrystallisation) recovered from the alkaline extract.

*Methylation.* A solution of the hydroxynaphthoxazole (1 g.) in chloroform (50 c.c.) was shaken with 30% aqueous potassium hydroxide (10 c.c.) and methyl sulphate (5 c.c.); the mixture was kept for 3 hours, warmed for 30 minutes, cooled, and kept overnight. *2-Keto-1-methyl-1 : 2-dihydro-β-naphthoxazole* crystallised from dilute methyl alcohol in needles, m. p. 188° (Found: C, 72·4; H, 4·55. $C_{12}H_9O_2N$ requires C, 72·4; H, 4·5%).

*2-Thiol-β-naphthoxazole.*—A mixture of the hydrochloride of 1-amino-2-naphthol (10 g.), carbon disulphide (20 c.c.), and potassium hydroxide (5 g.) in alcohol (100 c.c.) was heated under reflux for 12 hours, and an aqueous extract of the residue obtained by removal of alcohol and excess of carbon disulphide was acidified. On recrystallisation from dilute alcohol, the thiolnaphthoxazole was obtained in needles, m. p. 252°. Yield, 80%.

*Methylation.*—(i) Methyl iodide (1 c.c.) was gradually added to a solution of 2-thiol-β-naphthoxazole (1 g.) in methyl-alcoholic sodium methoxide (0·12 g. of sodium in 30 c.c. of absolute methyl alcohol); after 5 hours, the mixture was warmed for 20 minutes and kept overnight. The residue obtained after removal of methyl alcohol was extracted with water to remove sodium iodide and recrystallised from methyl alcohol, the S-*methyl* ether being obtained in long needles, m. p. 66—68° (Found: C, 66·6; H, 4·1; S, 14·9. $C_{12}H_9ONS$ requires C, 67·0; H, 4·2; S, 14·9%).

(ii) A solution of the thiolnaphthoxazole (1 g.) in chloroform (30 c.c.) was treated with 30% aqueous potassium hydroxide (10 c.c.) and thereafter with methyl sulphate (5 c.c.); the mixture was gently heated, kept overnight, and the excess of methyl sulphate destroyed with alkali. Extraction with chloroform furnished 2-methylthiol-β-naphthoxazole, which, after recrystallisation from methyl alcohol, had m. p. 66—68° alone and when mixed with the specimen already described.

*2-Thio-1-methyl-1 : 2-dihydro-β-naphthoxazole.*—An intimate mixture of 2-keto-1-methyl-1 : 2-dihydro-β-naphthoxazole (0·5 g.) and phosphorus pentasulphide (0·3 g.) was heated in an oil-bath at 170° for 8 hours, and the cooled melt was extracted with benzene. The *thiomethyldihydro*-derivative crystallised in small needles, m. p. 180° (Found: S, 14·9. $C_{12}H_9ONS$ requires S, 14·95%).

### *5-Bromobenzoxazoles.*

*5-Bromo-1-hydroxybenzoxazole.*—*Synthesis from 5-nitro-2-aminophenol.* Ethyl chloroformate (2·2 g.) was gradually added to 5-nitro-2-aminophenol (10 g.) in alcoholic sodium ethoxide (1·5 g. of sodium and 80 c.c. of absolute alcohol), and the mixture heated under reflux for 6 hours. The residue obtained by removal of alcohol was extracted with water to remove sodium chloride and then recrystallised from boiling water, *4-nitro-2-hydroxyphenylurethane*

being obtained in needles, m. p. 174° (Found: C, 47·7; H, 4·3. $C_9H_{10}O_5N_2$ requires C, 47·8; H, 4·4%). On dry distillation, this ester (which explodes on overheating) gave *5-nitro-1-hydroxybenzoxazole*, which crystallised from boiling water (containing a small amount of alcohol) in small lustrous needles, m. p. 244—246° (Found: C, 46·95; H, 2·3. $C_7H_4O_4N_2$ requires C, 46·7; H, 2·2%). Cyclisation was also effected by heating the nitrohydroxyphenylurethane at 180° for 30 minutes; the nitrohydroxybenzoxazole was isolated by extraction with 10% aqueous sodium hydroxide. A hot filtered solution of the nitrobenzoxazole in 10% aqueous sodium hydroxide was gradually treated with powdered sodium hyposulphite until the red colour disappeared. On cooling, *5-amino-1-hydroxybenzoxazole* separated as a mass of colourless crystals, which were washed with cold water and thereafter recrystallised from dilute alcohol; m. p. 204° (Found: C, 56·1; H, 3·85. $C_7H_6O_2N_2$ requires C, 56·0; H, 4·0%). The *acetyl* derivative, obtained by heating a solution of the base in acetic anhydride, crystallised from dilute alcohol in needles, m. p. 234° (Found: C, 56·3; H, 4·05. $C_9H_8O_3N_2$ requires C, 56·2; H, 4·2%). A mixture of copper sulphate (1·5 g.), sodium bromide (3 g.), copper turnings (1 g.), water (40 c.c.), and concentrated sulphuric acid (4 g.) was boiled under reflux until it was almost completely decolorised; 5-amino-1-hydroxybenzoxazole (1·5 g.) was then added to the mixture, which was cooled to 0° by addition of ice and gradually treated with a solution of sodium nitrite (1 g.) in cold water. The mixture was kept overnight and the precipitated *5-bromo-1-hydroxybenzoxazole* was washed with water and recrystallised from dilute alcohol, separating in needles (1·3 g.), m. p. 188—190° alone and when mixed with a specimen obtained by bromination of 1-hydroxybenzoxazole (Found: Br, 37·4. Calc. for $C_7H_4O_2NBr$: Br, 37·4%).

An attempt to hydrolyse 5-bromo-1-hydroxybenzoxazole with 25% aqueous sodium hydroxide proved unsuccessful, but on heating with concentrated hydrochloric acid under reflux for 14 hours the oxazole ring underwent fission. The basified and filtered solution gave on acidification with dilute hydrochloric acid the hydrochloride of 5-bromo-*o*-aminophenol, which crystallised from dilute alcohol in small needles, m. p. 290° (decomp.).

*Methylation.* A solution of the hydroxy-derivative (1 g.) in chloroform (15 c.c.) and 30% aqueous potassium hydroxide (5 c.c.) were treated with methyl sulphate (5 c.c.), kept for 4 hours, and gently warmed for 20 minutes. *5-Bromo-1-keto-2-methyl-1 : 2-dihydrobenzoxazole*, isolated by chloroform, crystallised from dilute alcohol in long needles, m. p. 150° (Found: Br, 35·1. $C_8H_6O_2NBr$ requires Br, 35·1%).

*Bromination of 1-Keto-2-methyl-1 : 2-dihydrobenzoxazole.*—A solution of the keto-derivative (1 g.) in chloroform (20 c.c.) was treated with bromine (1 g. in 5 c.c. of chloroform), and the mixture kept for 4 hours and then warmed. The product obtained by removal of chloroform was treated with sulphurous acid and recrystallised from alcohol, 5-bromo-1-keto-2-methyl 1 : 2-dihydrobenzoxazole being obtained, m. p. 149—150° alone and when mixed with the specimen already described.

*5-Bromo-1-thiolbenzoxazole.—Synthesis from 5-nitro-*o*-aminophenol.* *5-Nitro-1-thiolbenzoxazol* was prepared by heating a mixture of 5-nitro-*o*-aminophenol (10 g.), carbon disulphid (30 c.c.), and potassium hydroxide (10 g.) in alcohol (40 c.c.) under reflux for 10 hours. Th residue obtained by removal of alcohol and the excess of carbon disulphide was dissolved i water, and the filtered solution acidified, 5-nitro-1-thiolbenzoxazole being obtained, which o recrystallisation from dilute alcohol formed short needles, m. p. 216—218° (Found: S, 16· $C_7H_4O_3N_2S$ requires S, 16·3%). *5-Amino-1-thiolbenzoxazole* was obtained by treating a wan solution of the 5-nitro-compound (2 g.) in aqueous sodium hydroxide (1 g. in 30 c.c. of wate with sodium hyposulphite (3 g.) until the red colour was completely destroyed; the stra coloured needles which separated on cooling had m. p. 228° after recrystallisation from dilu alcohol (Found: S, 19·3. $C_7H_6ON_2S$ requires S, 19·3%). *5-Bromo-1-thiolbenzoxazole*, prepar from diazotised 5-amino-1-thiolbenzoxazole, separated from dilute alcohol in long needl m. p. 198—200° alone and when mixed with a specimen prepared by bromination of 1-thi benzoxazole (Found: Br, 34·7. Calc. for $C_7H_4ONBrS$: Br, 34·8%).

*Methylation.* (i) Methyl iodide (1 c.c.) was added to a solution of 5-bromo-1-thiolbenzoxaz (1·5 g.) in methyl-alcoholic sodium methoxide (0·2 g. of sodium and 30 c.c. of absolute metl alcohol) and the mixture was kept for 6 hours, heated on a water-bath for 45 minutes, and l overnight. The residue obtained on evaporation of methyl alcohol was treated with wat and the product crystallised from dilute methyl alcohol, *5-bromo-1-methylthiobenzoxazole* be obtained in long needles, m. p. 148° (Found: Br. 32·8. $C_8H_6ONBrS$ requires Br, 32·8 (ii) A solution of 5-bromo-1-thiolbenzoxazole (1 g.) in chloroform (10 c.c.) and 30% aque potassium hydroxide (12 c.c.) was methylated with excess of methyl sulphate. The *S*-met ether so obtained proved identical with that already described.

*Bromination of* 1-*Methylthiobenzoxazole*.—A solution of 1-methylthiobenzoxazole in chloroform (1 g. in 20 c.c.) was treated with bromine (1 g. in 5 c.c. of chloroform), and the mixture kept for some time. The residue obtained by removal of chloroform was treated with sulphurous acid and recrystallised from alcohol, 5-bromo-1-methylthiobenzoxazole being obtained, m. p. 148° alone and when mixed with a specimen obtained from methylation of 5-bromo-1-thiolbenzoxazole.

*Absorption Spectra of Benzselenazole Derivatives* (with ABDUL AZIZ FIRDAUS).

The measurements were made with a Carl Leiss spectrograph (type C), quartz absorption cells being used with a Wellington anti-screen plate, and a hydrogen tube which gave a constant source of light and enabled constant comparison spectra to be inserted between successive exposures with different cell thicknesses of solution. Juxtaposition was obtained by means of a Hartman diaphragm, and from the density matchpoints, molecular extinction coefficients followed.

An M/1000-solution of 1-hydroxybenzselenazole in absolute methyl alcohol was first examined and thereafter diluted to M/10,000 and then to M/100,000 with the same solvent. A similar procedure was followed with an M/1000-solution of 1-keto-2-methyl-1 : 2-dihydrobenzselenazole in methyl alcohol. An M/1000-solution of the hydroxyselenazole in N/100-aqueous sodium hydroxide was then examined and diluted with water first to M/10,000 and then to M/100,000. Similar experiments were carried out with 1-thiolbenzselenazole and 1-thio-2-methyl-1 : 2-dihydrobenzselenazole.

THE MUSLIM UNIVERSITY, ALIGARH, INDIA. [*Received, December 16th,* 1937.]

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## 66. *The Unsaturated Centre of the Triterpene Alcohol Lupeol.*

By I. M. HEILBRON, T. KENNEDY, and F. S. SPRING.

The monohydric triterpene alcohol lupeol, $C_{30}H_{50}O$, has been isolated in comparatively good yield from Mariposa gutta (*Palaquium leiocarpum*) and the presence of one ethylenic linkage and consequently its pentacyclic nature have been confirmed. Hydrogenation of lupenone gives the ketone lupanone, which is also obtained by the oxidation of lupanol. The presence of a methylene group adjacent to the carbonyl group in this saturated ketone has been demonstrated. The recognition of formaldehyde among the products from the ozonisation of lupenyl acetate shows that the ethenoid linkage is present as an exocyclic methylene group. From the behaviour of lupenyl acetate on oxidation with chromic anhydride, ozone, and hydrogen peroxide it is inferred that lupenol (lupeol) contains a bridge ring in the neighbourhood of the ethenoid linkage and thus differs from the triterpenes (hydropicene derivatives) previously examined in detail. This difference is reflected in the behaviour of lupenol on dehydrogenation, whereby 1 : 2 : 5-trimethylnaphthalene and possibly 1 : 2 : 5 : 6-tetramethylnaphthalene are obtained and not 1 : 2 : 7-trimethylnaphthalene or 1 : 8-dimethylpicene, two characteristic dehydrogenation products of the hydropicene group of triterpenes.

LUPEOL has been isolated from a variety of plant species; from *Sapotaceæ* (Tschirch and Schereschensky, *Arch. Pharm.*, 1905, **243**, 358; Cohen, *ibid.*, 1908, **246**, 520; Jungfleisch and Laroux, *Compt. rend.*, 1906, **142**, 1218; 1907, **144**, 1435; Romberg, *Ber.*, 1904, **37**, 3440; *Proc. K. Akad. Wetensch. Amsterdam*, 1905, **8**, 137; Heilbron, Moffet, and Spring, J., 1934, 1583), from *Rutaceæ* (Dieterle, *Arch. Pharm.*, 1919, **257**, 260; Oestling, *Ber. deut. Pharm. Ges.*, 1914, **24**, 308; Ultée, *Berlin Jardin. Bot. Buitenzorg*, 1922, [3], **4**, 315; Goodson, *Biochem. J.*, 1921, **15**, 123; Jones and White, *Amsterdam Sci. Abs.*, 1929, **42**, 49), and from *Leguminosæ* (Likienik, *Ber.*, 1891, **24**, 183, 2709; Schulze, *Z. physiol. Chem.*, 1904, **41**, 474).

We have now isolated it in relatively good yield from Mariposa gutta obtained from *Palaquium leiocarpum* (*Sapotaceæ*) " a large tree found only in Borneo, where it occurs on low-lying ground " (Gutta Percha, Malayan Series, No. XVIII, published by the Government of Malaya for the British Empire Exhibition).* Benzoylation of the non-saponifiable

* Private communication from the Director of the Imperial Institute, South Kensington, London.

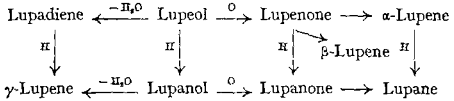
matter of the gutta gives a mixture, from which lupeol benzoate, m. p. 265°, is obtained as the least soluble component. The lupeol occurs in the gutta mainly as its cinnamate, since the latter is isolated from the alcoholic extract of the gutta in comparatively high yield.

Lupeol is a monohydric alcohol, $C_{30}H_{50}O$ (Nojd, *Arch. Pharm.*, 1927, **265**, 381); it contains one ethylenic linkage, since on hydrogenation it easily gives a saturated dihydro-derivative (Ruzicka, Huyser, Pfeiffer, and Seidel, *Annalen*, 1929, **471**, 21). This conclusion we have confirmed by a quantitative micro-catalytic hydrogenation and by a quantitative perbenzoic acid titration of lupeol acetate. Lupeol (lupenol) is therefore pentacyclic and in this respect differs from the sterols and resembles the majority of the triterpenes.

Hydrogenation of lupenyl acetate in presence of Adams's platinum oxide in glacial acetic acid yields *lupanyl acetate*, m. p. 245—246°, hydrolysis of which gives lupanol, m. p. 201—202° (*benzoate*, m. p. 259—260°), identical with that previously described by Ruzicka, Huyser, Pfeiffer, and Seidel (*loc. cit.*). Oxidation of lupanol with chromic anhydride gives mainly *lupanone*, m. p. 204—205°, together with a small amount of *lupanedicarboxylic acid*, m. p. 272°. Lupanone is also obtained in excellent yield by the catalytic hydrogenation of lupenone (Cohen, *Rec. trav. chim.*, 1909, **28**, 368) with Adams's platinum oxide as catalyst; it is characterised by the formation of a *hydrazone*, m. p. 341—342°, and a m-*nitrobenzylidene* derivative, m. p. 127°, the formation of the latter indicating the presence of the system $-CO-CH_2-$ in lupanone and consequently of the system $-CH(OH)-CH_2-$ in lupeol. Reduction of lupanone by either the Clemmensen or the Kishner–Wolff method gives *lupane*, m. p. 184°. Reduction of lupenone by the Kishner–Wolff process gives *α-lupene*, m. p. 163°, which is catalytically reduced to lupane, identical with that prepared from lupanone. When, however, lupenone is reduced by the Clemmensen method, an isomeric *β-lupene*, m. p. 191°, is formed which is resistant to catalytic hydrogenation.

Lupenone does not exhibit the typical selective absorption of an αβ-unsaturated ketone. A further proof that the ethenoid linkage is not in the αβ-position to the hydroxyl group is forthcoming in the observation that lupadiene, prepared by the dehydration of lupeol with phosphorus pentachloride (Nojd, *loc. cit.*), does not show selective absorption in the ultra-violet and hence cannot contain a conjugated system of ethylenic linkages. On catalytic reduction, lupadiene absorbs only one mole of hydrogen to give *γ-lupene*, m. p. 197—199°, which is also obtained by the dehydration of lupanol with phosphorus pentachloride and cannot be further hydrogenated.

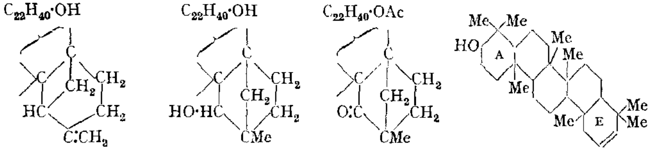
Ozonolysis of lupenyl acetate gives formaldehyde in 18% yield, characterised as its dimedon derivative, from which it follows that the ethenoid linkage of lupeol is present as an exocyclic methylene group. Ozonolysis of either β- or γ-lupene fails to give formaldehyde, whereas similar treatment of α-lupene gives this aldehyde, indicating that it is the parent hydrocarbon of lupeol.




With the object of examining the nature and location of the unsaturated centre of lupeol, the oxidation of lupenyl acetate has been investigated. Using chromic anhydride, Cohen (*loc. cit.*) isolated an acidic product which was not characterised; we obtained a similar product which is still being investigated. From the neutral fraction obtained by oxidation of lupenyl acetate with either chromic anhydride or ozone, we have isolated a monoacetate, $C_{32}H_{52}O_3$, m. p. 260—262°, which is unaltered by treatment with acetic anhydride and from which on hydrolysis an *alcohol*, $C_{30}H_{50}O_2$, m. p. 232°, is obtained. The acetate, which does not contain an active hydrogen atom (Zerewitinoff), is saturated (tetranitromethane in chloroform) and is extremely stable, being unaffected after prolonged treatment with chromic anhydride in boiling acetic acid. Although the acetate does not react with the usual carbonyl reagents, its ketonic character is revealed by spectroscopic examination. The presence of a carbonyl group has moreover been confirmed by reduction with sodium

and alcohol, a *dihydric alcohol*, $C_{30}H_{52}O_2$, m. p. 258°, being obtained which has been characterised by the formation of its *diacetate*, m. p. 238—239°.

An insight into the mechanism of formation of the saturated *keto-acetate*, m. p. 260—262°, has been obtained from a study of the action of hydrogen peroxide on lupenyl acetate. Hydrolysis of the crude reaction product gives a saturated dihydric alcohol identical with that obtained by reduction of the keto-acetate. Hydrogen peroxide, therefore, has effected the addition of a molecule of water, a reaction similar in all respects to the hydration of β-pinene to fenchyl alcohol (Henderson and Chisholm, J., 1924, **125**, 107). The behaviour of lupenyl acetate on oxidation thus allows us to give to lupeol the hypothetical partial structure (I), which adequately interprets the reactions involving the ethenoid linkage, the diol, m. p. 258°, being (II) and the keto-acetate (III). Lupeol thus differs from the triterpenes hitherto examined in detail (the oleanolic acid group) in that *it is not a derivative of hydropicene.*



(I.) (II.) (III.) (IV.)

*Note:* The investigations described in this communication have been in progress during the last three years. Since the section described above was completed a paper by Ruzicka, Furter, Pieth, and Schellenberg (*Helv. Chim. Acta*, 1937, **20**, 1564) has appeared in which the isolation of 1 : 2 : 5-trimethylnaphthalene and 6-hydroxy-1 : 2 : 5-trimethylnaphthalene from the dehydrogenation product of lupeol is described. We have made an incomplete study of the dehydrogenation of lupeol and have also isolated 1 : 2 : 5-trimethylnaphthalene together with a solid hydrocarbon which may be 1 : 2 : 5 : 6-tetramethylnaphthalene, but the amount available has not allowed a complete characterisation. A hypothetical formula (IV) for lupeol is advanced by Ruzicka in which this pentacyclic alcohol is represented as a derivative of the symmetrical, fully cyclised squalene, the ethenoid linkage being located in ring E. This formula will not give an interpretation of the results of oxidation of lupenyl acetate described above.

## Experimental.

*Isolation of Lupeol from Mariposa Gutta.*—The powdered gutta (1 kg.) was heated under reflux for 2 hours with successive portions of alcohol (3, 2, and 2 l.). The combined extract was cooled; the white solid (A) which then separated (270 g.; m. p. 135—145°) was hydrolysed by heating under reflux with alcoholic potassium hydroxide (2750 c.c.; 10%) for 3 hours. The solutiou was diluted with water (5 l.) and after 5 hours the coagulated white precipitate of non-saponifiable material was collected (200 g.; m. p. 145—150°). The non-saponifiable matter (150 g.) in benzene (150 c.c.) was treated with benzoyl chloride (95 g.) and pyridine (60 c.c.), and the mixture heated on the steam-bath for 10 hours. After removal of the solvents under reduced pressure the residue was triturated with methyl alcohol and then heated under reflux with acetone (1 l.) for ½ hour. After cooling and filtration, the solid was crystallised repeatedly from benzene–alcohol (1 : 3), from which lupenyl benzoate (31 g.) was obtained in large plates, $[\alpha]_D^{20°}$ + 60·1° * ($l$ = 1, $c$ = 3·02), m. p. 265°, which showed no depression on admixture with an authentic specimen (Found: C, 83·6; H, 10·1. Calc. for $C_{37}H_{54}O_2$: C, 83·7; H, 10·3%). Hydrolysis of the benzoate gave lupeol, which separated from dilute alcohol in long needles, $[\alpha]_D^{20°}$ + 26·4° ($l$ = 1, $c$ = 3·51), m. p. 211—212°, showing no depression in admixture with an authentic specimen (Found: C, 84·3; H, 11·7. Calc. for $C_{30}H_{50}O$: C, 84·4; H, 11·8%) and giving lupenyl acetate, m. p. 214—215°, $[\alpha]_D^{20°}$ + 47·3° ($l$ = 1, $c$ = 2·33), on acetylation.

*Microhydrogenation.* A solution of the lupenyl acetate (11·02 mg.) in glacial acetic acid in

* All rotations were measured in chloroform solution.

the presence of platinum-black absorbed 0·595 c.c. of hydrogen at 20·7° and 749 mm., corresponding to 1·04 double bonds. *Perbenzoic acid titration:* After 24 and 48 hours the acetate (0·1560 g.) in chloroform solution had absorbed the equivalent of 4·8 mg. and 4·85 mg. respectively of oxygen, corresponding to 0·90 and 0·91 ethylenic linkage.

*Lupenyl Cinnamate from Mariposa Gutta.*—The solid (A) was crystallised four times from acetone; the product, m. p. 195—206°, after repeated crystallisation from benzene–alcohol, attained the constant m. p. 234—235°, not depressed by authentic lupenyl cinnamate (Cohen, *loc. cit.*) (Found: C, 84·1; H, 10·1. Calc. for $C_{39}H_{56}O_2$: C, 84·1; H, 10·1%).

*Lupanyl Acetate.*—A solution of lupenyl acetate (5·5 g.) in glacial acetic acid (150 c.c.) was shaken with hydrogen and Adams's platinum oxide catalyst (0·3 g.) at 70° for 3 hours. The solution was filtered, and the product precipitated with water and crystallised twice from alcohol; *lupanyl acetate* then separated in triangular plates (5·0 g.), m. p. 245—246°, $[\alpha]_D^{20°} - 1·8°$ ($l = 1$, $c = 7·21$) (Found: C, 81·7; H, 11·5. $C_{32}H_{54}O_2$ requires C, 81·6; H, 11·6%). Hydrolysis of the acetate with alcoholic potassium hydroxide gave lupanol, which crystallised from alcohol in needles, m. p. 201—202°, $[\alpha]_D^{20°} - 17·8°$ ($l = 1$, $c = 2·84$) (Found: C, 83·9; H, 12·2. Calc. for $C_{30}H_{52}O$: C, 84·0; H, 12·2%). *Lupanyl benzoate* separated from benzene–alcohol (1 : 3) in hexagonal plates, m. p. 259—260°, $[\alpha]_D^{20°} + 27·1°$ ($l = 1$, $c = 3·37$) (Found: C, 83·1; H, 10·7. $C_{37}H_{56}O_2$ requires C, 83·4; H, 10·6%). Neither lupanol nor its derivatives gave a coloration with tetranitromethane in chloroform solution.

*Lupanone.*—(a) Lupenone, prepared by Cohen's method (*loc. cit.*), separated from alcohol in large hard needles, m. p. 169·5—170·5°, $[\alpha]_D^{20°} + 63·5°$ ($l = 1$, $c = 1·63$) (Found: C, 84·9; H, 11·4. Calc. for $C_{30}H_{48}O$: C, 84·8; H, 11·4%). It was characterised by the preparation of the *hydrazone*, which separated from aqueous alcohol either in plates or in needles, m. p. 341—342° (decomp.), the two forms being interconvertible (Found: C, 82·0; H, 11·7; N, 6·2. $C_{30}H_{50}N_2$ requires C, 82·1; H, 11·5; N, 6·4%). Lupenone (5·0 g.) was hydrogenated by the method adopted for the preparation of lupanyl acetate. *Lupanone* separated from alcohol in plates, m. p. 204—205°, $[\alpha]_D^{20°} + 16·2°$ ($l = 1$, $c = 1·76$) (Found: C, 84·2; H, 11·8. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). The *oxime* separated from ethyl acetate in long fine needles, m. p. 270° (Found: C, 81·3; H, 11·5; N, 3·1. $C_{30}H_{51}ON$ requires C, 81·5; H, 11·6; N, 3·2%). *Lupanonehydrazone* separated from alcohol–nitrobenzene (2 : 1) in needles, m. p. 341—342° (decomp.) (Found: C, 81·4; H, 11·7; N, 6·2. $C_{30}H_{52}N_2$ requires C, 81·7; H, 11·9; N, 6·35%). A solution of the ketone (0·7 g.) and *m*-nitrobenzaldehyde (0·62 g.) in glacial acetic acid (20 c.c.) and chloroform (12·5 c.c.) was saturated with dry hydrogen chloride at 0°. After standing at room temperature for 3 days, the mixture was washed successively with water, aqueous sodium hydroxide, and water. Removal of the solvent from the dried solution, followed by crystallisation of the residue from alcohol, gave the m-*nitrobenzylidene* derivative of lupanone in pale yellow needles, m. p. 127° (Found: C, 79·0; H, 9·9; N, 2·8. $C_{37}H_{53}O_3N$ requires C, 79·4; H, 9·5; N, 2·5%).

(b) Lupanol (2·85 g.) in glacial acetic acid (230 c.c.) was treated with a solution of chromic anhydride (3 g.) in water (5 c.c.), and glacial acetic acid (35 c.c.) added slowly with shaking during 15 minutes. The mixture was heated on the steam-bath for 2 hours, diluted with water, and extracted with ether. The ethereal solution was washed with potassium hydroxide solution (10%) (extract A) and then with water. After removal of ether from the dried solution the residue was crystallised thrice from alcohol to give lupanone, m. p. 204—205°, identical with the specimen prepared by method (a). Extract A was acidified with dilute sulphuric acid, and the solution extracted with ether. The acidic fraction, isolated in the usual manner, was crystallised twice from aqueous acetic acid and twice from alcohol; *lupanedicarboxylic acid* was then obtained in microscopic plates, m. p. 272° (decomp.) (Found: C, 75·4; H, 10·6. $C_{30}H_{50}O_4$ requires C, 75·9; H, 10·6%).

*α-Lupene.*—Lupenonehydrazone (2·7 g.) was heated with a solution of sodium ethoxide (from 1·7 g. of sodium) in alcohol (20 c.c.) for 8 hours in a sealed tube at 180°. The mixture was diluted with water, and the precipitated solid collected and crystallised twice from dilute alcohol; *α-lupene* then separated in hard needles (0·7 g.), m. p. 163°, $[\alpha]_D^{20°} + 30·2°$ ($l = 1$, $c = 3·56$), which gave a yellow coloration with tetranitromethane in chloroform solution (Found: C, 87·65; H, 12·2. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%).

*Lupane.*—(a) α-Lupene (0·25 g.) in ethyl acetate (150 c.c.) was shaken at 40° with hydrogen for 3 hours, Adams's platinum oxide (0·05 g.) being used as catalyst. After two crystallisations from ethyl alcohol the product gave *lupane* in long needles, m. p. 184°, $[\alpha]_D^{20°} - 1·1°$ ($l = 1$, $c = 8·33$), which did not give a coloration with tetranitromethane in chloroform solution (Found: C, 87·2; H, 12·7. $C_{30}H_{52}$ requires C, 87·3; H, 12·7%).

(b) Lupanone (2·0 g.) in glacial acetic acid (200 c.c.) was heated under reflux for 10 hours with amalgamated zinc (20 g.) and concentrated hydrochloric acid (50 c.c.), added in five equal portions at intervals of 2 hours. After decantation, the solution was diluted with water, and the mixture extracted with ether. The product, isolated in the usual manner, was repeatedly crystallised from alcohol to give lupane in long hard needles, m. p. 184°, identical with that prepared by method (a).

(c) Lupanonehydrazone (1·8 g.) was heated for 8 hours at 180° in a sealed tube with a solution of sodium ethoxide (from 1·1 g. of sodium) in alcohol (15 c.c.). The product was diluted with water, and the precipitated solid collected and crystallised thrice from alcohol to give lupane (0·5 g.), m. p. 184°, not depressed by the specimens prepared by methods (a) and (b).

β-*Lupene*.—Lupenone (2 g.) was reduced under the conditions described for the preparation of lupane [method (b)]. After many crystallisations from methyl alcohol–ether, β-*lupene* was obtained in small needles (0·05 g.), m. p. 191°, $[\alpha]_D^{20°}$ + 21·4° ($l$ = 1, $c$ = 0·627), giving a yellow colour with tetranitromethane in chloroform solution (Found: C, 87·6; H, 12·2. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%).

γ-*Lupene*.—(a) Lupadiene prepared by Nojd's method (*loc. cit.*) had m. p. 175°, $[\alpha]_D^{20°}$ + 24·6° ($l$ = 1, $c$ = 1·07) (Found: C, 88·0; H, 12·0. Calc. for $C_{30}H_{48}$: C, 88·1; H, 11·9%). Lupadiene (1·0 g.) in ethyl acetate (150 c.c.) was shaken with hydrogen and Adams's platinum oxide catalyst (0·15 g.) at 40° for 3 hours. Removal of the solvent, followed by crystallisation of the residue from ether–alcohol and then from ethyl acetate, gave γ-*lupene* in large hard needles, m. p. 197—199°, $[\alpha]_D^{20°}$ − 19·7° ($l$ = 1, $c$ = 3·25). The product gave a yellow coloration with tetranitromethane in chloroform solution (Found: C, 87·6; H, 12·3. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%).

(b) Lupanol (1·5 g.) was added in small portions to a suspension of phosphorus pentachloride in light petroleum (b. p. 40—60°; 25 c.c.) during 4 hours. The mixture was heated under reflux for 30 minutes, cooled, and washed repeatedly with water. After removal of the solvent from the dried solution, the residue was crystallised repeatedly from alcohol–ether, from which γ-lupene separated in short hard needles (0·6 g.), m. p. 197—199°, identical with the specimen prepared by method (a).

*Keto-acetate*, $C_{32}H_{52}O_3$ (III).—(a) Lupenyl acetate (10 g.) in acetic acid (300 c.c.) was treated with a solution of chromic anhydride (10 g.) in acetic acid (80 c.c.) and water (7 c.c.), added with stirring during 1 hour at 90°. The mixture was heated under reflux for a further 2 hours, and the solvent then removed under reduced pressure and, after the addition of water, repeatedly extracted with ether. The ethereal solution was washed with dilute sulphuric acid and then with aqueous potassium hydroxide (5%). The insoluble potassium salt separating was removed and washed with ether, the washings being added to the ethereal solution. This was dried (sodium sulphate), and the solvent evaporated; the residue (2·5 g.), m. p. 228—232°, gave, after repeated crystallisation from ethyl alcohol, the *keto-acetate* (0·7 g.) in hard needles, m. p. 260—262°, $[\alpha]_D^{20°}$ + 7·4° ($l$ = 1, $c$ = 1·1) (Found: C, 79·2; H, 11·1. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). *Light absorption in alcohol:* Maximum, approx. 2800 A., ε = 60.

(b) Lupenyl acetate (10 g.) in chloroform (80 c.c.) was treated with a slow stream of ozonised oxygen (6%) at room temperature for 6 hours. The solvent was removed under reduced pressure, and the hard white ozonide decomposed by heating under reflux with water for 1 hour. The mixture was then distilled in steam, and the steam-volatile constituents collected in water. This aqueous distillate was treated with an alcoholic solution of dimedon; the formaldehyde dimedon derivative obtained (1·12 g.) had m. p. 183—185°, not depressed by an authentic specimen.

An ethereal solution of the non-volatile residue was washed successively with aqueous potassium hydroxide (10%) and water. Removal of the solvent from the dried solution gave a white solid (2·5 g.), which after many crystallisations from ethyl alcohol was obtained in hard needles, m. p. 260—262°, showing no depression on admixture with a specimen prepared by method (a).

*Keto-alcohol*, $C_{30}H_{50}O_2$, *m. p.* 232°.—The keto-acetate (III) (0·35 g.) was heated under reflux with an excess of alcoholic potassium hydroxide (10 c.c.; 5%) for 4 hours. The solid separating, on cooling was crystallised from alcohol, from which the *keto-alcohol* separated in needles, m. p. 232°, $[\alpha]_D^{20°}$ − 13·2° ($l$ = 1, $c$ = 2·3) (Found: C, 81·6; H, 11·1. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). *Light absorption in alcohol:* Maximum, 2750 A., ε = 53.

*Dihydric Alcohol*, $C_{30}H_{52}O_2$ (II).—(a) Lupenyl acetate (10 g.) in acetic acid (250 c.c.) was treated with hydrogen peroxide (Merck's perhydrol; 25 c.c.). The mixture was heated on the steam-bath for 2 hours and largely diluted with water, and the solid collected and hydrolysed

by heating under reflux for 2 hours with an excess of alcoholic potassium hydroxide (5%). The product was isolated by water precipitation and crystallised from alcohol and then repeatedly from ethyl acetate, from which the *diol* separated in long needles, m. p. 258° (Found: C, 81·2; H, 11·5. $C_{30}H_{52}O_2$ requires C, 81·0; H, 11·8%). *Active hydrogen determination* (*Zerewitinoff*): 6·353 Mg. gave 0·75 c.c. of methane, measured at 0° and 760 mm., corresponding to 2·2 atoms of active hydrogen. The *diacetate* was prepared by treatment with acetic anhydride and pyridine and separated from methyl alcohol in plates, m p. 238—239° (Found: C, 77·5; H, 10·4. $C_{34}H_{56}O_4$ requires C, 77·2; H, 10·7%). Neither the diacetate nor the diol gave a coloration with tetranitromethane in chloroform solution.

(b) A boiling solution of the keto-acetate (III) (1 g.) in alcohol (50 c.c.) was treated with sodium (4 g.), added as rapidly as the reaction would permit. After dilution with alcohol (20 c.c.) a further addition of sodium (2 g.) was made, and the mixture was then heated under reflux for 1 hour and diluted with water. The solid obtained was washed with water and crystallised from alcohol and then from ethyl acetate, from which the diol separated in needles, m. p. 258° either alone or in admixture with the specimen described under (a). Acetylation gave the diacetate, m. p. 238—239°, showing no depression on admixture with that prepared by method (a).

Our thanks are due to Dr. W. McMeeking for his help in the earlier stages of this investigation and to Imperial Chemical Industries Ltd. for a grant.

The University, Manchester. [*Received, January 22nd, 1938.*]

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## 67. *Studies in the Sterol Group. Part XXXV. The Bromination of 7-Ketocholestanyl Acetate.*

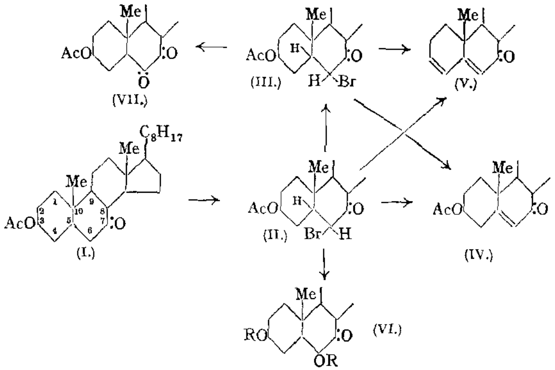
By T. Barr, I. M. Heilbron, E. R. H. Jones, and F. S. Spring.

In continuation of our study of the bromination of steroid ketones, which has as its ultimate object the preparation of heavily unsaturated derivatives, an investigation of 7-ketocholestanyl acetate has been undertaken. Two monobromides were obtained with one mole of bromine and shown to be stereoisomeric 6-bromo-7-ketocholestanyl acetates.

In contradistinction to 6-ketocholestanyl acetate (Heilbron, Jones, and Spring, J., 1937 801; Heilbron, Jackson, Jones, and Spring, this vol., p. 102) the isomeric 7-ketocholestany acetate (I) is not brominated in acetic acid at room temperature. In chloroform at roor temperature with one mole of bromine, however, α-6-*bromo-7-ketocholestanyl acetate* (II m. p. 173—175°, is obtained, the constitution of which is established by its facile conversio into 7-keto-3-acetoxy-$\Delta^5$-cholestene (IV) and 7-keto-$\Delta^{3:5}$-cholestadiene (V) on treatmer with pyridine. Hydrolysis of the monobromide with methyl-alcoholic potassium hydroxic gives 3 : 6-dihydroxy-7-ketocholestane (VI, R = H), characterised as a disecondar alcohol by its *dibenzoate* (VI, R = COPh), m. p. 184—186°. Both from the mother-liqu of the monobromide, m. p. 173—175°, and also by the action of hydrogen bromide on t α-monobromide the isomeric β-6-*bromo-7-ketocholestanyl acetate* (III), m. p. 142—143°, obtained, which with pyridine likewise gives (IV) and (V), the elimination of hydrog bromide, however, being effected in this case only with difficulty. The difference orientation of the halogen atom in the two new monobromides is clearly illustrated by th reactions with silver nitrate and pyridine. Whereas the α-isomer readily gives the u saturated ketone (IV), the β-bromide gives 6 : 7-diketocholestanyl acetate (VII), a behavic reminiscent of the stable 7-bromo-6-ketocholestanyl acetate (Heilbron, Jones, and Spri *loc. cit.*), and which we again attribute to an inherent difficulty of removal of hydro halide, with consequent tendency to hydrolysis and oxidation. These results would app to indicate that in the α-isomer the hydrogen attached to $C_5$ and the $C_6$ bromine atom *cis*-oriented and that in the β-bromide the *trans*-orientation obtains.

Treatment of 7-ketocholestanyl acetate with two moles of bromine or of either of monobromides with one mole of bromine in the presence of hydrogen bromide, give

*dibromide*, m. p. 176—177°. The formation of this compound from 7-ketocholestanyl acetate must proceed *via* the α-6-monobromide, followed by isomerisation to the β-isomeride. This is shown by the fact that, when one mole of bromine and one mole of hydrogen bromide are used, the velocity of bromination of the α-monobromide is markedly less than in the case of its stereoisomer. The dibromide does not react with *o*-phenylenediamine in alcohol and only unworkable gels are obtained by the action of pyridine, pyridine and silver nitrate, methyl-alcoholic potassium hydroxide and potassium acetate in alcohol.




An observation of some interest is revealed by a consideration of the ultra-violet absorption spectra of the mono- and di-bromo-substitution products of 6- and 7-ketocholestanyl acetates :—

| | Maximum, A. | Log ε. |
|---|---|---|
| 7-Ketocholestanyl acetate | 2870 | 1·6 |
| α-6-Bromo-7-ketocholestanyl acetate | 3130 | 2·2 |
| β-6-Bromo-7-ketocholestanyl acetate | 2820 | 1·6 |
| Dibromo-7-ketocholestanyl acetate | 3040 | 2·2 |
| 6-Ketocholestanyl acetate | 2800 | 1·6 |
| 5-Bromo-6-ketocholestanyl acetate | 3080 | 2·1 |
| 7-Bromo-6-ketocholestanyl acetate | 3100 | 2·2 |
| 5 : 7-Dibromo-6-ketocholestanyl acetate | 3400 | 2·2 |
| 5′ : 7-Dibromo-6-ketocholestanyl acetate | 3050 | 2·1 |

A marked displacement of the absorption band due to the carbonyl group by the introduction of a bromine atom in the α-position is only observed when the halogen atom has a particular steric arrangement. Thus in the case of 7-ketocholestanyl acetate the band at 2870 A. is displaced to 3130 A. in α-6-bromo-7-ketocholestanyl acetate, but no such effect is observed in the case of the β-isomer. This phenomenon becomes especially clear from a consideration of the isomeric dibromides of 6-ketocholestanyl acetate (Heilbron, Jackson, Jones, and Spring, *loc. cit.*). In the case of 5 : 7-dibromo-6-ketocholestanyl acetate, the observed single displacements (approximately 300 A.) of the 5- and 7-monobromides are additive in effect; on the other hand, the 5′ : 7-isomer exhibits only a single displacement due to the effect of the $C_7$ halogen atom, the bromine at $C_{5'}$ being without optical influence.

## Experimental.

*7-Ketocholestanyl Acetate* (cf. Windaus and Kirchner, *Ber.*, 1920, **53**, 614).—A suspension of 7-keto-3-acetoxy-$\Delta^5$-cholestene (10 g.) in acetic acid (120 c.c.) was shaken with palladium-norit and hydrogen until absorption of gas was complete. The solution was filtered and diluted

with water, and the solid crystallised from ether–methyl alcohol, from which 7-ketocholestanyl acetate (9·8 g.) separated in lustrous plates, m. p. 142—143°.

*Reduction of 7-Ketocholestanol to Cholestanol.*—The observation that both 6- and 7-ketocholestanes give the same dicarboxylic acid on oxidation (Windaus, *Ber.*, 1920, **53**, 496) indicates that rings A and B in the two ketones have the same relative configuration. It is conceivable, however, that during such an oxidation inversion of $C_5$ may have occurred. We have now shown that 7-ketocholestanyl acetate is a derivative of cholestane and not of coprostane, since reduction by the Wolff–Kishner method, *via* the semicarbazone, gives cholestanol. A solution of 7-ketocholestanol (Windaus and Kirchner, *loc. cit.*) (3·2 g.) in hot alcohol (50 c.c.) was treated with alcoholic semicarbazide acetate, and the mixture set aside at room temperature for 60 hours. The crude semicarbazone obtained by addition of water was crystallised once from alcohol and, after drying, the solid (2·8 g.) was heated at 190° in a sealed tube for 7 hours with sodium ethoxide in alcohol (25 c.c.; 20%). The reaction mixture was treated with water, and the product isolated with ether. Trituration of the residual gum with acetone gave a solid (1·2 g.), two crystallisations of which from alcohol yielded cholestanol (0·6 g.), m. p. 141°, not depressed on admixture with an authentic specimen.

*α-6-Bromo-7-ketocholestanyl Acetate* (II).—7-Ketocholestanyl acetate (5 g.) in chloroform (30 c.c.) was treated at 20° with a freshly prepared solution of bromine in chloroform (13 c.c.; 15%). The mixture was stirred throughout the addition, which extended over 5 minutes, the chloroform removed under reduced pressure, and the residual solid triturated with acetone and filtered. After one crystallisation from the same solvent *α-6-bromo-7-ketocholestanyl acetate* (2·8 g.) separated in thick plates, m. p. 173—175°, $[\alpha]_D^{19°} + 35°$ ($l = 1$, $c = 1·0$ in chloroform) (Found: C, 66·8; H, 9·1. $C_{29}H_{47}O_3Br$ requires C, 66·5; H, 9·1%).

*β-6-Bromo-7-ketocholestanyl Acetate* (III).—(a) The first acetone mother-liqnor of α-6-bromo-7-ketocholestanyl acetate was evaporated and the solid obtained was repeatedly crystallised from dilute acetic acid to give *β-6-bromo-7-ketocholestanyl acetate* (1 g.) in leaflets, m. p. 142—143°, $[\alpha]_D^{19°} - 8·8°$ ($l = 1$, $c = 1·0$ in chloroform) (Found: C, 66·5; H, 9·0%).

(b) α-6-Bromo-7-ketocholestanyl acetate (0·5 g.) in acetic acid (50 c.c.) was treated with a solution of hydrogen bromide in acetic acid (5 c.c.; 50%), and the mixture heated on the steam-bath for 15 minutes, the colour of the solution passing through red to a deep brown. The oil precipitated with water was isolated by ether extraction and taken up in hot aqueous acetic acid; β-6-bromo-7-ketocholestanyl acetate separated in leaflets, m. p. 142—143°, not depressed by the specimen prepared by method (a).

*Treatment of α- and β-6-Bromo-7-ketocholestanyl Acetates with Pyridine.*—A solution of α-6-bromo-7-ketocholestanyl acetate (1·0 g.) in anhydrous pyridine (10 c.c.) was heated under reflux for 6 hours. The cold solution was diluted with water and the product, isolated with ether, was crystallised from methyl alcohol, yielding 7-keto-3-acetoxy-$\Delta^5$-cholestene, m. p. 155—156° either alone or in admixture with an authentic specimen. From the mother-liquor, 7-keto-$\Delta^{3:5}$-cholestadiene was isolated, m. p. 110—112°, giving no depression with an authentic specimen and exhibiting the typical light absorption in alcohol (maximum, 2800 A.). In the case of β-6-bromo-7-ketocholestanyl acetate a satisfactory elimination of hydrogen bromide was only effected if the treatment with pyridine was continued for at least 8 hours. After this time 7-keto-3-acetoxy-$\Delta^5$-cholestene and 7-keto-$\Delta^{3:5}$-cholestadiene were isolated and identified as described above.

*7-Keto-3 : 6-dibenzoyloxycholestane.*—α-6-Bromo-7-ketocholestanyl acetate (0·9 g.) was heated under reflux with methyl-alcoholic potassium hydroxide (30 c.c.; 10%) for 2 hours. Addition of water to the reaction mixture gave a gum, which was isolated by means of ether and solidified on boiling with methyl alcohol. The keto-diol separated from methyl alcohol in leaflets, softening at 140°, m. p. 148—150°. When it was kept at room temperature for 18 hours with beuzoyl chloride and pyridine, *7-keto-3 : 6 dibenzoyloxycholestane* was obtained; this crystallised from acetone–methyl alcohol in small prisms, softening at 182°, m. p. 184—186° (Found: C, 78·4; H, 8·7. $C_{41}H_{54}O_5$ requires C, 78·5; H, 8·7%).

*Treatment of α- and β-6-Bromo-7-ketocholestanyl Acetates with Silver Nitrate and Pyridine.*—A solution of either α- or β-6-bromo-7-ketocholestanyl acetate (1·0 g.) and silver nitrate (2·0 g.) in anhydrous pyridine (20 c.c.) was heated under reflux for 5 hours. Ether was added to the cold solution, which was then washed with dilute sulphuric acid and water. In the case of the α-isomer the product obtained after removal of the ether readily crystallised from methyl alcohol, yielding 7-keto-3-acetoxy-$\Delta^5$-cholestene, m. p. 156—157° both alone and in admixture with an authentic specimen. In the case of the β-isomer removal of the ether gave a gum, which solidified after trituration with methyl alcohol, repeated crystallisation from the same solvent

yielding 6 : 7-diketocholestanyl acetate (100 mg.) in needles, m. p. 156—157°, showing no depression when mixed with an authentic specimen, and giving the characteristic quinoxaline derivative, m. p. 184—186°.

*Dibromo-7-ketocholestanyl Acetate.*—(a) A freshly prepared solution of bromine in chloroform (13 c.c.; 15%; 2·0 mols.) was added at 20° to a solution of 7-ketocholestanyl acetate (2·5 g.) in chloroform (25 c.c.) during 40 minutes. After being set aside at room temperature for 48 hours, the reaction mixture was washed with aqueous sodium bicarbonate and dried, the chloroform removed under diminished pressure, and the residue crystallised. *Dibromo-7-ketocholestanyl acetate* (1·6 g.) separated from acetone or light petroleum (b. p. 40—60°) in plates, m. p. 176—177°, $[\alpha]_D^{19°}$ + 38·1° ($l$ = 1, $c$ = 2·9 in chloroform) (Found: C, 57·7; H, 7·5. $C_{29}H_{46}O_3Br_2$ requires C, 57·8; H, 7·7%).

(b) A solution of α-6-bromo-7-ketocholestanyl acetate (2·0 g.) in acetic acid (350 c.c.) and ether (100 c.c.) was treated with a solution of bromine in acetic acid (13 c.c.; 5%; 1 mol.) and a solution of hydrogen bromide in acetic acid (5 c.c.; 50%; 8 mols.). After the mixture had been set aside at room temperature for 48 hours, dibromo-7-ketocholestanyl acetate separated, and a further quantity was obtained by dilution with water and extraction with ether (total yield, 0·75 g.); m. p. 176—177°, not depressed by a specimen prepared by method (a).

(c) A solution of β-6-bromo-7-ketocholestanyl acetate (1 g.) in acetic acid (40 c.c.) was treated with a solution of bromine in acetic acid (6·5 c.c.; 5%; 1·0 mol.) and a solution of hydrogen bromide in acetic acid (0·3 c.c.; 50%; 1 mol.), the mixture then being set aside at room temperature for 48 hours. Dibromo-7-ketocholestanyl acetate separated and after crystallisation from acetone (0·8 g.) had m. p. 176—177° both alone and in admixture with an authentic specimen.

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The University, Manchester. [*Received, January 22nd,* 1938.]

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## 68. *Some Addition Reactions of the Azomethinic Group.*

By D. Philpott and W. J. Jones.

The reactivity of the azomethinic group in anils and indolenines has been investigated. It has been found that aldehyde-anils are more reactive than ketone-anils or benzoyleneindolenines, although methyleneaniline stands alone in that it does not combine with acid chlorides or with acetoacetic ester. Of the aldehyde-anils investigated, the most reactive are benzylideneaniline and benzylidene-β-naphthylamine, cinnamylideneaniline having somewhat lower additive power.

The addition compound of benzylideneaniline with acetyl chloride has been investigated by Garzarolli-Thurnlackh (*Ber.*, 1899, **32**, 2277), and that of benzylideneaniline with benzoyl chloride by him and by James and Judd (J., 1914, **105**, 1427). On hydrolysis these addition compounds yield the original aldehyde, hydrogen chloride, and the acyl or aroyl derivative of the original amine. Very similar in properties to these addition compounds is that formed by benzylideneaniline with acetic anhydride, which on hydrolysis gives benzaldehyde, acetic acid, and acetanilide. According to Leuchs and Winzer (*Ber.*, 1925, **58**, 1522), Leuchs with Philpott, Sander, Heller, and Köhler (*Annalen*, 1928, **461** 27) and Leuchs, Wulkow, and Gerland (*Ber.*, 1932, **65**, 1586) addition of acid anhydrides and acyl halides to indolenines occurs at the azomethinic group, *viz.*,

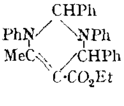
$$:C(O{\cdot}COR){\cdot}N(COR){\cdot} \text{ and } :CCl{\cdot}N(COR){\cdot}.$$

By the action of benzylideneaniline on acetoacetic ester, Schiff and Bertini (*Ber.*, 1897, **30**, 601; 1898, **31**, 207, 601) obtained the α-(α′-anilinobenzyl)acetoacetic ester,

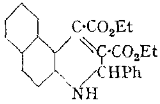
$$CHPh(NHPh){\cdot}CH(CO{\cdot}CH_3){\cdot}CO_2Et.$$

This ester occurs in keto- and enolic forms, and by treating the latter with acetic acid and alcohol Bertini (*Gazzetta*, 1899, **29**, 22) obtained a *m*-diazine derivative (I), containing two

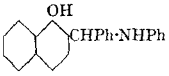
benzylideneaniline groups to one of acetoacetic ester. Benzylidene-β-naphthylamine and oxalacetic ester (Simon and Conduche, *Compt. rend.*, 1904, **139**, 297) combine, molecule for molecule, to give α-(α′-2-naphthylaminobenzyl)oxalacetic ester, which on treatment with concentrated sulphuric acid condenses to a cyclic substance (II).



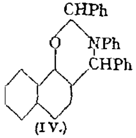
(I.)



(II.)



(III.)



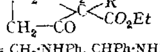
(IV.)

In a similar way, some of the anils combine with naphthols, which potentially contain an enolic group, *e.g.*, benzylideneaniline and α-naphthol form the substance (III) (Betti and Speroni, *Gazzetta*, 1900, **30**, 301). The compounds formed are capable of reacting with aldehydes, and in this way Betti prepared (*ibid.*, 1901, **31**, 377) a naphthoxazine derivative (IV) from the compound of benzylideneaniline and α-naphthol by condensation with benzaldehyde. Betti further found that the addition compounds of anils with naphthols reacted with phenylhydrazine, with substitution of the phenylhydrazine radical for that of aniline.

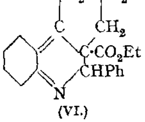
The effect of substituents in the anil on the stability of the acetyl and benzoyl compounds, of the type described by Garzarolli-Thurnlackh and by James and Judd (*loc. cit.*), has now been investigated, and it has been found that the compounds of the anils of benzaldehyde, acetophenone, benzophenone, cinnamaldehyde, and those of benzylidene-β-naphthylamine are readily formed, but that methyleneaniline does not combine with either acetyl or benzoyl chloride. These compounds are insoluble in non-polar solvents and are immediately resolved into their generators, or derivatives thereof, by hydroxylic solvents.

Maleic anhydride has been found to yield with the same anils, including methyleneaniline, the monoanilide of maleic acid and the original aldehyde or ketone. Phthalic anhydride similarly gives the monoanilide of phthalic acid and benzaldehyde in the case of benzylideneaniline.

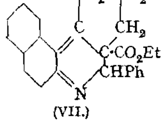
The initial addition compounds given by methyleneaniline, by benzylideneaniline, and by benzylidene-β-naphthylamine with ethyl*cyclo*pentan-1-one-2-carboxylate, *viz.*, *ethyl 2-anilinomethyl*cyclo*pentan-1-one-2-carboxylate* (V), *ethyl 2-α-anilinobenzyl*cyclo*pentan-1-one-2-carboxylate* (V), and *ethyl 2-α-2′-naphthylaminobenzyl*cyclo*pentan-1-one-2-carboxylate* (V), respectively, have been found to be of the type described by Schiff and Bertini (*loc. cit.*). The structure assigned to this type by these authors is confirmed by the fact that benzylideneaniline and the disubstituted ketonic ester, ethyl 2-methyl*cyclo*pentan-1-one-2-carboxylate, do not react together. It has also been found that the ketone-anils, *e.g.*, those of acetophenone and benzophenone, do not combine with ethyl *cyclo*pentan-1-one-2-carboxylate. The compounds formed by benzylideneaniline and by benzylidene-β-naphthylamine, on treatment with acetic acid and alcohol according to the procedure of Bertini (*loc. cit.*), yield by loss of water, respectively, *ethyl 2-phenyl-3 : 4-trimethylene-2 : 3-dihydroquinoline-3-carboxylate* (VI) and *ethyl 3-phenyl-1 : 2-trimethylene-2 : 3-dihydro-β-naphthaquinoline-2-carboxylate* (VII).



(V; R = $CH_2{\cdot}NHPh$, $CHPh{\cdot}NHPh$, or $CHPh{\cdot}NH{\cdot}C_{10}H_7$.)



(VI.)

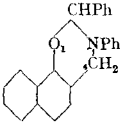


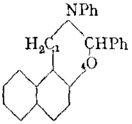
(VII.)

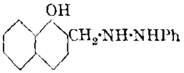
These products are for the most part recovered unchanged after treatment with 50% sulphuric acid, iodine, acetic anhydride, methyl iodide or phenylhydrazine, but with

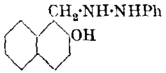
picric acid they give the picrate of the original anil. It has also been found that Bertini's *m*-diazine derivative (I) similarly yields the picrate of benzylideneaniline. Structurally these products resemble the cyclic substance (II) of Simon and Conduche. Ethyl 2-anilinomethyl*cyclo*pentan-1-one-2-carboxylate (V) does not condense on treatment with acetic acid and alcohol, which is reminiscent of the fact that the Doebner synthesis of quinolines frequently fails in the case of formaldehyde and of methylal (Claus and Brandt, *Annalen*, 1894, **282**, 93; Pictet and Misner, *Ber.*, 1912, **45**, 1800).

Addition compounds, 2-*anilinomethyl*-1-*naphthol*, 1-*anilinomethyl*-2-*naphthol*, and 1-α-*anilinocinnamyl*-2-*naphthol*, of the type of those of Betti and Speroni (III), are formed by methyleneaniline and by cinnamylideneaniline with the naphthols, but not by the anils of acetophenone and benzophenone. Of these, the methyleneaniline addition compounds, but not that of cinnamylideneaniline, condense with benzaldehyde to form 2 : 3-*diphenyl*-2 : 3-*dihydro*-1 : 3-α-*naphthoxazine* (VIII) and 2 : 3-*diphenyl*-2 : 3-*dihydro*-2 : 4-β-*naphthoxazine* (IX).


(VIII.)

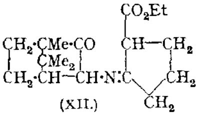

(IX.)

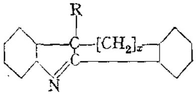

(X.)

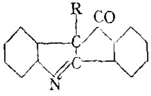

(XI.)

The addition compounds formed by methyleneaniline with the naphthols yield monoacetyl derivatives with acetic anhydride, and with phenylhydrazine they give 2-*phenylhydrazinomethyl*-1-*naphthol* (X) and 1-*phenylhydrazinomethyl*-2-*naphthol* (XI), of the type obtained by Betti (*loc. cit.*).

The anilic compound *ethyl 2-camphoryliminocyclopentane-1-carboxylate* (XII), obtained by condensation of α-aminocamphor and ethyl *cyclo*pentan-1-one-2-carboxylate, gives no reaction with acetic anhydride.


(XII.)


(XIII.)


(XIV; R = Me or Ph.)

Leuchs and his co-workers (*loc. cit.*) have found that in indolenines of the general formula (XIII) the azomethinic group, when $x = 1$, *i.e.*, in hydrindenes, adds on acid anhydrides, acid chlorides, and, in some cases, also phenylhydrazine, but that, when $x = 2$, the azomethinic group is inactive. In the present work we have found that, with a hydrindone ring present, *e.g.*, in 3-*methyl*-2 : 3-o-*benzoyleneindolenine* (XIV) and 3-*phenyl*-2 : 3-o-*benzoyleneindolenine* (XIV), the azomethinic group fails to form addition products with acid anhydrides, with acid halides, with phenylhydrazine, or with hydroxylamine.

The low activity of methyleneaniline cannot be entirely attributed to its existence in the polymeric form (von Miller and Plöchl, *Ber.*, 1892, **25**, 2021), since it has here and elsewhere been shown that it is capable of entering into reaction, and that, when it does so, it functions in its monomeric form, even in the cold, *e.g.*, it gives anilinoacetonitrile with hydrogen cyanide (von Miller and Plöchl, *loc. cit.*) and *NN'*-diphenyl-*NN'*-methyleneurea with phenyl *iso*cyanate (Senier and Shepheard, J., 1909, **95**, 504).

## Experimental.

*Ethyl 2-anilinomethyl*cyclo*pentan-1-one-2-carboxylate* (V), rectangular plates, m. p. 53° (Found: C, 69·0; H, 7·5; N, 5·7. $C_{15}H_{19}O_3N$ requires C, 68·9; H, 7·3; N, 5·4%), is formed by refluxing (20 mins.) methyleneaniline (10 g.), ethyl *cyclo*pentan-1-one-2-carboxylate (14·9 g.),

and alcohol (130 c.c.), concentrating the solution in a vacuum, and recrystallising the product from ligroin (yield, 21 g.). It gives, both in benzene and in alcohol, an orange-yellow coloration, changing to reddish-violet, with ferric chloride.

*Ethyl 2-α-anilinobenzyl*cyclo*pentan-1-one-2-carboxylate* (V), needles, m. p. 88° (Found: C, 74·7; H, 6·9; N, 4·0. $C_{21}H_{23}O_3N$ requires C, 74·8; H, 6·8; N, 4·2%), and *ethyl 2-α-2'-naphthylaminobenzyl*cyclo*pentan-1-one-2-carboxylate* (V), needles, m. p. 111° (Found: C, 77·7; H, 6·5. $C_{25}H_{25}O_3N$ requires C, 77·5; H, 6·5%), are obtained similarly, the former from benzylideneaniline (18·1 g.) and alcohol (75 c.c.) (yield, 27 g.), the latter from benzylidene-β-naphthylamine (23·1 g.) and benzene (80 c.c.) (yield 17 g.), with, in each case, ethyl *cyclo*pentan-1-one-2-carboxylate (15·6 g.). Both give a reddish-violet coloration with ferric chloride.

*Ethyl 2-phenyl-3 : 4-trimethylene-2 : 3-dihydroquinoline-3-carboxylate* (VI), bright yellow needles, m. p. 102° (Found: C, 79·0, 78·8; H, 6·7, 6·6; N, 4·4, 4·3; *M*, cryoscopic in benzene, 291. $C_{21}H_{21}O_2N$ requires C, 79·0; H, 6·6; N, 4·4%; *M*, 319) (yield, 7 g.), and *ethyl 3-phenyl-1 : 2-trimethylene-2 : 3-dihydro-β-naphthaquinoline-2-carboxylate* (VII), bright yellow needles, m. p. 130° (Found: C, 81·2; H, 6·3; N, 4·0; *M*, in benzene, 354. $C_{25}H_{23}O_2N$ requires C, 81·3; H, 6·2; N, 3·8%; *M*, 369) (yield, 8 g.), are obtained by refluxing (15 mins.), with glacial acetic acid (70 c.c.), and absolute alcohol (70 c.c.), ethyl 2-α-anilinobenzyl*cyclo*pentan-1-one-2-carboxylate (14 g.) and ethyl 2-α-2'-naphthylaminobenzyl*cyclo*pentan-1-one-2-carboxylate (16 g.), respectively. These two substances are also obtained, in even better yield, by refluxing ethyl *cyclo*pentan-1-one-2-carboxylate (1 mol.), glacial acetic acid, absolute alcohol, and either benzylideneaniline (1 mol.) or benzylidene-β-naphthylamine (1 mol.), without isolation of the intermediate addition compounds. Further, it has been found that Bertini's *m*-diazine derivative (I) can be obtained in good yield by the direct action of glacial acetic acid and absolute alcohol on a mixture of benzylideneaniline and acetoacetic ester.

*2-Anilinomethyl-1-naphthol*, rhombic prisms, m. p. 117° (Found: C, 81·8; H, 6·3; N, 5·6%), and *1-anilinomethyl-2-naphthol*, needles, m. p. 132° (Found: C, 81·6; H, 6·3; N, 5·7. $C_{17}H_{15}ON$ requires C, 81·9; H, 6·0; N, 5·6%), are formed by allowing a solution of methyleneaniline (2·3 g.) and either α- or β-naphthol (3·1 g.) in benzene (16 c.c.) to stand (2 days), diluting it, after concentration, with ligroin, and recrystallising the product from ligroin–benzene. Their benzene solutions give a reddish-violet coloration with ethereal ferric chloride. Similarly obtained, from cinnamylideneaniline (4·3 g.) and β-naphthol (3·1 g.) after a week, the oily solid precipitated on dilution with ligroin being pressed on porous earthenware and recrystallised from benzene, *1-α-anilinocinnamyl-2-naphthol*, needles, m. p. 218° (Found: C, 85·5; H, 6·1; N, 4·1. $C_{25}H_{21}ON$ requires C, 85·5; H, 6·0; N, 4·0%), gives no coloration with ferric chloride. The *monoacetyl* derivative of 2-anilinomethyl-1-naphthol, needles, m. p. 127° (Found: C, 78·1; H, 6·0; N, 5·0%), and the *monoacetyl* derivative of 1-anilinomethyl-2-naphthol, rectangular plates, m. p. 176° (Found: C, 78·2; H, 6·0; N, 4·8. $C_{19}H_{17}O_2N$ requires C, 78·3; H, 5·8; N, 4·8%), give no coloration with ferric chloride.

*2-Phenylhydrazinomethyl-1-naphthol* (X), yellow needles, m. p. 106° (Found: N, 10·7%), and *1-phenylhydrazinomethyl-2-naphthol* (XI), yellow needles, m. p. 206° (decomp.) (Found: N, 9·8. $C_{17}H_{16}ON_2$ requires N, 10·6%), separate when hot mixtures of the corresponding anilinomethyl compounds with phenylhydrazine in alcohol are cooled; they are recrystallised from alcohol.

*2 : 3-Diphenyl-2 : 3-dihydro-1 : 3-α-naphthoxazine* (VIII), prisms, m. p. 150° (Found: C, 85·5; H, 5·8; N, 4·2%), and *2 : 3-diphenyl-2 : 3-dihydro-2 : 4-β-naphthoxazine* (IX), prisms, m. p. 140° (Found: C, 85·6; H, 5·8; N, 4·1. $C_{24}H_{19}ON$ requires C, 85·5; H, 5·6; N, 4·2%), are best obtained by heating together at 110° (5 mins.) the parent anilinomethyl compounds (1 mol.) with benzaldehyde (1 mol.), washing the products with absolute alcohol, and recrystallising them from ligroin–benzene. They may also be prepared directly by keeping an alcoholic solution of methyleneaniline (1 mol.), the corresponding naphthol (1 mol.), and benzaldehyde (2 mols.) for a week. In benzene these oxazines give a reddish-brown coloration with ethereal ferric chloride.

*Ethyl 2-camphoryliminocyclopentane-1-carboxylate* (XII), needles, m. p. 129° (Found: C, 70·8; H, 9·0; N, 4·6. $C_{18}H_{27}O_3N$ requires C, 70·8; H, 8·9; N, 4·6%), is obtained by refluxing (2 hours) a solution of α-aminocamphor (6·0 g.), ethyl *cyclo*pentan-1-one-2-carboxylate (5·6 g.), and sodium acetate (5·0 g.) in 75% aqueous acetic acid (36 g.), diluting the solution with water, taking up the precipitated oil in ether, separating, drying, and concentrating the ethereal solution, and recrystallising the product from alcohol (yield, 3·1 g.). It gives yellow colorations in alcohol both with ferric chloride and with sodium ethoxide.

*3-Methyl-2 : 3-o-benzoyleneindolenine* (XIV), yellow rhombic prisms, m. p. 175° (Found : C, 82·4; H, 4·8; N, 6·2; *M*, in benzene, 241. $C_{16}H_{11}ON$ requires C, 82·4; H, 4·7; N, 6·0%; *M*, 233), and *3-phenyl-2 : 3-o-benzoyleneindolenine* (XIV), fine yellow needles, m. p. 225° (Found : C, 85·3; H, 4·6; N, 4·8; *M*, in benzene, 307. $C_{21}H_{13}ON$ requires C, 85·4; H, 4·4; N, 4·7%; *M*, 295), are obtained by refluxing (3 hours) the parent monophenylhydrazone of 1 : 3-diketo-2-methylhydrindene (4 g.) (Wislicenus and Kötze, *Annalen*, 1889, **252**, 81) and the monophenylhydrazone of 1 : 3-diketo-2-phenylhydrindene (5 g.) (Nathanson, *Ber.*, 1893, **26**, 2576), respectively, anhydrous zinc chloride (32 g.), and absolute alcohol (20 c.c.), twice washing the product with cold dilute N-hydrochloric acid, drying, extracting impurities with warm alcohol, and recrystallising the residual benzoyleneindolenine from ligroin–benzene (yields, 1·5 g. and 1·7 g.).

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## 69. *The Oxidation of Certain Alkyl Tellurides.*

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From di-*n*-butyl telluride and the ethyl and the *l*-menthyl ester of *n*-butyltelluroacetic acid, by interaction with alkyl halides or by oxidation under acid conditions, telluronium compounds are obtained which are readily soluble in organic solvents and have definite melting points. Oxidation of the three tellurides under neutral conditions gives *n*-butyltellurinic acid or products which contain this acid associated with telluroxides : these are all insoluble or only sparingly soluble in organic solvents and have no true melting points, but decompose between 180° and 220°. Oxidation of *l*-menthyl tellurodiacetate by neutral hydrogen peroxide gives a compound of the telluronium type, formed by combination of the telluroxide with hydrogen peroxide.

The decomposition of aliphatic telluroxides which results in the formation of *n*-butyltellurinic acid is discussed. The suggestion is made that this acid exists as polymerides, and that telluroxide molecules may be associated with these polymerides in such a way as to prevent the decomposition of the telluroxide.

DI-*n*-BUTYL TELLURIDE, prepared by a method similar to that used by Tschugaev and Chlopin (*J. Russ. Phys. Chem. Soc.*, 1915, **47**, 364) for the preparation of alkyl selenides, combines with methyl iodide and with certain substituted alkyl bromides to give crystalline telluronium halides, (XII)—(XV) in the table. By thermal decomposition of (XIII) and (XIV) the unsymmetrical aliphatic tellurides *ethyl* n-*butyltelluroacetate* and l-*menthyl* n-*butyltelluroacetate* respectively are obtained, which give the crystalline *telluronium bromides* (XVI) and (XVII) by combination with ω-bromoacetophenone.

Like tellurodiacetic and ditellurodiacetic acid (Morgan and Drew, J., 1925, **127**, 531), dimethyl telluride (Vernon, J., 1920, **117**, 889), di-*p*-anisyl ditelluride (Morgan and Kellett, J., 1926, 1080), *cyclo*telluropentane (Morgan and Burgess, J., 1928, 321), and *cyclo*tellurobutane (Morgan and Burstall, J., 1931, 180), these two unsymmetrical tellurides, as well as di-*n*-butyl telluride, are oxidised when exposed to air in the homogeneous state or in solution. They are also readily oxidised by nitric acid or by hydrogen peroxide.

The compositions of the oxidation products isolated are given in the table. In most cases, oxidation by air or hydrogen peroxide under neutral conditions gives the expected telluroxide associated with *n*-butyltellurinic acid, but only n-*butyltellurinic acid* (I) was isolated from the products of the action of air, or of hyperol (urea perhydrate) in ethyl-alcoholic solution, on *l*-menthyl *n*-butyltelluroacetate.

When the tellurides are oxidised under acid or alkaline conditions, simple derivatives of quadrivalent tellurium are obtained. For example, the oxidation of di-*n*-butyl telluride and of *l*-menthyl *n*-butyltelluroacetate by dilute nitric acid yields the corresponding *hydroxy-nitrates* (X), (XI), and alkaline hydrogen peroxide oxidises di-*n*-butyl telluride to the *dihydroxide* (VIII). The oxidation of *l*-menthyl *n*-butyltelluroacetate by benzoyl peroxide gives a compound which may be formed by the union of one molecule of *l*-menthyl *n*-butyltelluroxyacetate with two molecules of benzoic acid. Our analyses of this compound suggest that it is formed with elimination of water, and that it is the

*dibenzoyl* derivative of the dihydroxide of *l*-menthyl *n*-butyltelluroacetate (IX), analogous to the diacetyldiarylselenonium compounds described by Foster (*Rec. trav. chim.*, 1935, **54**, 446).

*Oxidation Products and Telluronium Compounds derived from Di-*n*-butyl Telluride and the Ethyl and* l*-Menthyl Esters of* n*-Butyltelluroacetic Acid.*

| From | Reagent. | Product. | | Decomp. temp. or m. p. |
|---|---|---|---|---|
| $Bu{\cdot}Te{\cdot}CH_2{\cdot}CO_2C_{10}H_{19}$ | air | $Bu{\cdot}TeO{\cdot}OH$ | (I) | decomp. 220° |
| ,, | hyperol | ,, | | ,, |
| $TeBu_2$ | air | $TeBu_2O,3Bu{\cdot}TeO{\cdot}OH$ | (II) | decomp. 180 |
| $Bu{\cdot}Te{\cdot}CH_2{\cdot}CO_2Et$ | ,, | $Bu{\cdot}TeO{\cdot}CH_2{\cdot}CO_2Et,2Bu{\cdot}TeO{\cdot}OH$ | (III) | decomp. 185 |
| ,, | $H_2O_2$ | ,, | | ,, |
| (XI) | $NHEt_2$ | $Bu{\cdot}TeO{\cdot}CH_2{\cdot}CO_2H,2Bu{\cdot}TeO{\cdot}OH$ | (IV) | decomp. 210 |
| $Bu{\cdot}Te{\cdot}CH_2{\cdot}CO_2C_{10}H_{19}$ | $H_2O_2$ | $Bu{\cdot}TeO{\cdot}CH_2{\cdot}CO_2C_{10}H_{19},Bu{\cdot}TeO{\cdot}OH$ | (V) | decomp. 210 |
| $TeBu_2$ | ,, | $2TeBu_2O,Bu{\cdot}TeO{\cdot}OH$ | (VI) | decomp. 180 |
| (V) | $HNO_3$ | $Bu{\cdot}TeO{\cdot}O{\cdot}TeBu(NO_3){\cdot}CH_2{\cdot}CO_2C_{10}H_{19}$ | (VII) | decomp. 130 |
| $TeBu_2$ | alkaline $H_2O_2$ | $TeBu_2(OH)_2$ | (VIII) | decomp. 120 |
| $Bu{\cdot}Te{\cdot}CH_2{\cdot}CO_2C_{10}H_{19}$ | benzoyl peroxide | $Bu{\cdot}Te(O{\cdot}COPh)_2{\cdot}CH_2{\cdot}CO_2C_{10}H_{19}$ | (IX) | m. p. 133 |
| $TeBu_2$ | $HNO_3$ | $TeBu_2(OH){\cdot}NO_3$ | (X) | m. p. 84 |
| $Bu{\cdot}Te{\cdot}CH_2{\cdot}CO_2C_{10}H_{19}$ | ,, | $Bu{\cdot}Te(OH)(NO_3){\cdot}CH_2{\cdot}CO_2C_{10}H_{19}$ | (XI) | m. p. 42 |
| $TeBu_2$ | MeI | $TeMeBu_2I$ | (XII) | m. p. 159 |
| ,, | $CH_2Br{\cdot}CO_2Et$ | $TeBu_2Br{\cdot}CH_2{\cdot}CO_2Et$ | (XIII) | m. p. 63 |
| ,, | $CH_2Br{\cdot}CO_2C_{10}H_{19}$ | $TeBu_2Br{\cdot}CH_2{\cdot}CO_2C_{10}H_{19}$ | (XIV) | m. p. 90 |
| ,, | $CH_2Br{\cdot}COPh$ | $TeBu_2Br{\cdot}CH_2{\cdot}COPh$ | (XV) | m. p. 87 |
| $Bu{\cdot}Te{\cdot}CH_2{\cdot}CO_2Et$ | ,, | $TeBuBr(CH_2{\cdot}CO_2Et){\cdot}CH_2{\cdot}COPh$ | (XVI) | m. p. 89 |
| $Bu{\cdot}Te{\cdot}CH_2{\cdot}CO_2C_{10}H_{19}$ | ,, | $TeBuBr(CH_2{\cdot}CO_2C_{10}H_{19}){\cdot}CH_2{\cdot}COPh$ | (XVII) | m. p. 106 |

On account of their limited solubility, *n*-butyltellurinic acid and the complex products (II)—(VI) cannot be recrystallised. It is, however, suggested that (II)—(VI) are compounds, not only on account of the improbability that mixtures of the two components would separate in an amorphous infusible state in consistently simple proportions, but also because they cannot be readily separated into telluroxides and *n*-butyltellurinic acid. For example, (V) loses up to 40% in weight on trituration with aqueous sodium carbonate, but no precipitate is obtained on neutralisation or acidification of the extract. When (V) is treated with nitric acid, the *n*-butyltellurinic acid which it contains is not converted into a soluble nitrate. A new substance is obtained which contains equimolecular proportions of *l*-menthyl *n*-butyltelluroxyacetate, *n*-butyltellurinic acid, and nitric acid and is probably best formulated with elimination of water, as the l-*menthyl* ester of *n*-buty *n*-butyltellurinyltelluretine nitrate (VII), analogous to the dibenzoyl derivative (IX) The action of diethylamine on the hydroxy-nitrate (XI) also indicates that telluroxide cannot be isolated readily from the compounds which they form with acids. The remova of nitric acid by the amine is accompanied by hydrolysis and oxidation of the telluroxide the product of the reaction being a substance (IV) which contains *n*-butyltelluroxyaceti acid and *n*-butyltellurinic acid.

The simple telluronium compounds (IX)—(XVII) melt between 42° and 159° and ar all readily soluble in one or more solvents. The complex compounds (II)—(VI), on the othe hand, have no true melting points, but decompose between 180° and 220° and are insolubl or only sparingly soluble in most organic solvents. *n*-Butyltellurinic acid (I), (II), an (IV) are sparingly soluble only in boiling ethyl alcohol, (III) and (VI) are somewha more soluble in boiling ethyl alcohol [the solution of (VI) gelates on cooling], and onl (V) is soluble in cold ether, chloroform and carbon disulphide.

*n*-Butyltellurinic acid, in its infusibility and sparing solubility, resembles pheny tellurinic acid (Lederer, *Ber.*, 1915, **48**, 1345), but is in contrast to the recorded alky sulphinic and -seleninic acids, all of which melt below 140° and are readily soluble in number of organic solvents. The properties of *n*-butyltellurinic acid suggest that it exis as a polymeride. Two modes of polymerisation present themselves, hydrogen-bo formation, and the formation of a covalency between the telluroxide oxygen of one molecu and the tellurium of another. The latter structure, in harmony with the infusibility of t acid, is the more likely, involving the expansion of the outer shell of the tellurium at to ten electrons. Patry (*Compt. rend.*, 1935, **201**, 71) has concluded that telluric a

($H_2TeO_4$) exists as polymerides; this structure, if confirmed, would be analogous to that now postulated for *n*-butyltellurinic acid.

The formation of tellurinic acids in the oxidation of dialkyl tellurides is due to the instability of the telluroxides which are the primary oxidation products. These decompose into butane-1-tellurol and an aldehyde, which in the presence of excess of the oxidising agent are converted into *n*-butyltellurinic acid and a carboxylic acid respectively (*n*-butyric acid was isolated as a by-product of the oxidation of di-*n*-butyl telluride by hydrogen peroxide). Many aliphatic sulphoxides and most aliphatic selenoxides decompose in a similar manner (Edwards, Gaythwaite, Kenyon, and Phillips, J., 1928, **2293**; Larsson and Jönsson, *Ber.*, 1934, **67**, 2003). Sulphinic and seleninic acids can be isolated in simple forms, but the lesser stability of quadrivalent tellurium compounds would cause monomeric alkyltellurinic acids to decompose by further enolisation. As a polymeride, telluric acid cannot enolise, and hence is sufficiently stable to be isolated.

The formation of (II)—(VI), by oxidation under neutral conditions, is then to be attributed to the instability of alkyl telluroxides, which results in the formation of *n*-butyltellurinic acid, and to the tendency of the tellurinic acid so formed to polymerise and to become associated with the telluroxide by oxygen-tellurium bonds. The association of a number of molecules in this way, either by ring formation or by extensive linear polymerisation, would prevent the enolisation which leads to decomposition of the telluroxides and tellurinic acid. Alkaline or acid conditions of oxidation result in the formation of the dihydroxide (VIII), or derivatives of dihydroxides (IX), (X), (XI), in which enolisation is impossible, so these compounds are comparatively stable and of simple constitution.

The present experiments suggest that dialkyl telluroxides cannot be isolated from the oxidation products of dialkyl tellurides; few well-characterised dialkyl telluroxides are described in the literature. The dimethyl and diethyl telluroxides described by Mallet (*Annalen*, 1851, **79**, 223) and Wohler and Dean (*Annalen*, 1855, **93**, 235) were probably dihydroxides, since they were obtained by the actiou of silver oxide on the corresponding dihalides in aqueous solution, and the recorded properties of *cyclo*tellurobutane 1-oxide (Morgan and Burgess, J., 1931, 182) are consistent with the suggestion that it was a complex substance analogous to those described above. Diaryl selenoxides (Edwards, Gaythwaite, Kenyon, and Phillips, *loc. cit.*) are more stable than dialkyl selenoxides and it is therefore likely that telluroxides of the diaryl series would be more stable than those of the dialkyl series. Lederer (*Annalen*, 1912, **391**, 326; *Ber.*, 1916, **49**, 334, 1071, 1615, 2552; 1920, **53**, 1674) obtained eleven diaryl telluroxides which had melting points ranging from 154° to 225° and were readily soluble in organic solvents.

Drew (J., 1929, 560) has shown that during the evaporation, on the steam-bath, of an aqueous solution of dimethyltelluronium dihydroxide a mixed anhydride of trimethyltelluronium hydroxide and methyltellurinic acid is formed, from which trimethyltelluronium iodide and methyltelluronium tri-iodide are obtained on treatment with hydriodic acid. By the action of hydriodic acid on (II), (III), and (VI), *di*-n-*butyltelluronium di-iodide* and n-*butyltelluronium tri-iodide* are obtained, but tri-*n*-butyltelluronium iodide could not be identified amongst the products. It may therefore be inferred that migration of *n*-butyl radicals does not occur during the formation of the substances (II)—(VI). Mixtures of di-*n*-butyltelluronium di-iodide and *n*-butyltelluronium tri-iodide are also formed during the interaction of iodine with di-*n*-butyl telluride in carbon tetrachloride solution or with ethyl *n*-butyltelluroacetate in ethereal solution and by the interaction of hydriodic acid and di-*n*-butyltelluronium dihydroxide in acetone solution. The tri-iodide is also formed by the action of hydriodic acid in acetone solution on the di-iodide. The general reactions which lead to the formation of mixtures of the di- and tri-iodides are:

$$(1)\quad TeR'I + RI \longleftarrow TeRR'I_2 \longrightarrow TeRI + R'I.$$
$$(2)\quad TeRI + I_2 \longrightarrow TeRI_3.$$
$$(3)\quad TeRI + RI \longrightarrow TeR_2I_2.$$
$$(4)\quad R{\cdot}TeO{\cdot}OH + 3HI \longrightarrow TeRI_3 + 3H_2O.$$

Reactions of types (1), (2), and (4) have been observed by Edwards, Gaythwaite, Kenyon, and Phillips (*loc. cit.*) with *p*-tolylselenoacetic acid dibromide, *p*-bromoselenotoluene, and

*p*-tolueneseleninic acid respectively, and of type (4) by Drew (*loc. cit.*) with methyltellurinic acid.

The l-*menthyl* ester of tellurodiacetic acid is obtained as a higher-boiling fraction in the thermal decomposition of the *l*-menthyl ester of di-*n*-butyltelluretine bromide. By oxidation of the *l*-menthyl ester in acetone solution with hydrogen peroxide, a compound, m. p. 90°, is obtained which is readily soluble in organic solvents, and is further distinguished from the products (I)—(VI) in that it oxidises hydriodic acid and rapidly decolorises aqueous potassium permanganate. The analysis of this substance agrees with that of a hydrated tellurone; it is therefore similar in properties and composition to the compound, described as a hydrated tellurone, which Morgan and Burgess (*loc. cit.*) obtained on oxidation of *cyclo*telluropentane. The results described above, however, suggest that tellurone formation would be preceded by extensive oxidation of the alkyl groups attached to the tellurium atom, and that products analogous to (I)—(VI), containing tellurinic acids, would be expected to be present in the oxidation products. The absence of such compounds suggests that the telluroxide, which is the primary product of the oxidation of *l*-menthyl tellurodiacetate, is stabilised by combination with hydrogen peroxide, forming a derivative analogous to the dihydroxide (VIII) and the hydroxy-nitrates (X), (XI). On this basis the compound obtained by oxidation of the *l*-menthyl ester is a ***hydroxy-perhydrate*** $(CH_2{\cdot}CO{\cdot}O{\cdot}C_{10}H_{19})_2Te(OH){\cdot}O{\cdot}OH$, and the compound which Morgan and Burgess described as a tellurone may be formulated in the same way as $C_5H_{10}{>}Te(OH){\cdot}O{\cdot}OH$. This suggestion is in agreement with the analyses of these two compounds and provides a better explanation of their oxidising action than does the assumption that tellurones are oxidising agents. The impure explosive dimethyltellurone (Found: C, 10·5; H, 3·2. Calc.: C, 12·7; H, 3·2%) described by Vernon (J., 1920, **117**, 889) was probably a similar compound (dimethyltelluroxyperhydrate, $C_2H_7O_3Te$, requires C, 11·2; H, 3·4%), mixed or in association with the complex $TeMe_2O,Me{\cdot}TeO_2H$ ($C_3H_{10}O_3Te_2$ requires C, 10·3; H, 2·9%).

## Experimental.

Equivalent weights were determined by refluxing 0·1—0·3 g. of the substance in 0·05N-alcoholic potassium hydroxide and back titration with 0·1N-hydrochloric acid. The calculated values are g. of substance which would react with 56 g. of potassium hydroxide by neutralisation of acid groups and saponification of ester groups, in the formulæ proposed.

*Di*-n-*butyl Telluride*.—To a warmed solution of tellurium (40 g.), sodium formaldehyde sulphoxylate ("rongalite," 90 g.), and sodium hydroxide (70 g.) in water (400 c.c.), *n*-butyl bromide (90 g.) in ethyl alcohol (350 c.c.) was slowly added with stirring, under reflux, a current of coal gas being passed through the apparatus. Di-*n*-butyl telluride (45 g.), isolated by extraction with ether, drying with calcium chloride, and removal of the ether, was stored under coal gas. After three redistillations it had b. p. 109—112°/12 mm., $d_{4°}^{25°}$ 1·2923, $n_D^{19°}$ 1·518. The telluride reacted with an equimolecular proportion of ω-bromoacetophenone, giving crystalline phenacyl-di-*n*-butyltelluronium bromide (XV), m. p. 87°, and with bromoacetic acid, giving a viscous uncrystallisable product.

*Methyldi*-n-*butyltelluronium Iodide* (XII).—A mixture of di-*n*-butyl telluride (12·1 g., 1 mol.) and methyl iodide (8·0 g., 1 mol.) became warm and rapidly set to a solid mass, which was washed with dry ether and recrystallised from chloroform. The product, ***methyldi*-n-*butyltelluronium iodide*** (16 g.), m. p. 159° (decomp.), was soluble in water (Found: C, 27·6; H, 5·0; I, 32·[illegible]; Te, 33·6. $C_9H_{21}ITe$ requires C, 28·2; H, 5·5; I, 33·1; Te, 33·3%).

l-*Menthyl Ester of Di*-n-*butyltelluretine Bromide* (XIV).—A mixture of *l*-menthyl bromoacetate (41·5 g., 1 mol.) and di-*n*-butyl telluride (36 g., 1 mol.) crystallised rapidly. After recrystallisation from ether–light petroleum, the *l*-menthyl ester of di-*n*-butyltelluretine bromide (62 g.) was obtained, m. p. 90°, $[\alpha]_{5461}^{17·5°}$ − 23·6° in chloroform (*l*, 2; *c*, 2·5), soluble in cold water, decomposed by hot water.

*Ethyl Ester of Di*-n-*butyltelluretine Bromide* (XIII).—A mixture of di-*n*-butyl telluride (24 g., 1 mol.) and ethyl bromoacetate (16·7 g., 1 mol.) crystallised rapidly. The solid was washed with light petroleum and recrystallised from chloroform–light petroleum. The ***ethyl*** ester of di-*n*-butyltelluretine bromide (35 g.), m. p. 62°, was soluble in ether and in water (Found: C, 35·2; H, 6·0; Te, 31·2. $C_{12}H_{25}O_2BrTe$ requires C, 35·3; H, 6·2; Te, 31·2%).

*Ethyl* n-*Butyltelluroacetate*.—The preceding ethyl ester (15 g.) decomposed on distillation

under reduced pressure, the first fraction being *n*-butyl bromide and the second *ethyl* n-*butyltelluroacetate*, which after redistillation had b. p. 135—138°/21 mm., 85°/< 0·1 mm., $n_D^{18°}$ 1·5276 (Found: C, 36·3; H, 6·3; Te, 47·3. $C_8H_{16}O_2Te$ requires C, 35·4; H, 6·0; Te, 47·0%). The ester was stored under coal gas; yield, 8 g. The ester (4·2 g., 1 mol.) combined with ω-bromoacetophenone (3·0 g., 1 mol.) on gentle warming; *from the product, by trituration with anhydrous* ether and recrystallisation from chloroform–ethyl alcohol, the *ethyl* ester of phenacyl-*n*-butyltelluretine bromide (XVI) (0·3 g.) was obtained, m. p. 89°; it was soluble in acetone (Found: C, 40·5; H, 5·0; Te, 27·4. $C_{16}H_{23}O_3BrTe$ requires C, 40·8 H, 4·9; Te, 27·1%).

l-*Menthyl* n-*Butyltelluroacetate*.—The *l*-menthyl ester of di-*n*-butyltelluretine bromide (40 g.) decomposed at 100°/20 mm. with evolution of *n*-butyl bromide. The residue, distilled at < 0·1 mm., yielded l-*menthyl* n-*butyltelluroacetate* (18 g.), which after redistillation had b. p. 120—125°/0·1 mm., $[\alpha]_{5461}^{20°}$ − 5·2° (*l*, 0·5), $d_4^{20°}$ 1·2515, $n_D^{20°}$ 1·5182 (Found: C, 50·2; H, 7·9; Te, 33·4. $C_{16}H_{30}O_2Te$ requires C, 50·3; H, 7·9; Te, 33·4%). The ester was stored under coal gas. The ester (12·4 g., 1 mol.) combined with ω-bromoacetophenone (6·5 g., 1 mol.) on gentle warming: the product was washed with anhydrous ether and recrystallised from chloroform–ethyl alcohol. The l-*menthyl* ester of phenacyl-*n*-butyltelluretine bromide (XVII) (12·3 g.) *obtained had m. p.* 106°, $[\alpha]_{5461}^{20°}$ − 23·7° *in chloroform* (*l*, 2; *c*, 4·5), and was *soluble in* chloroform, insoluble in ethyl alcohol, acetone, and ether (Found: C, 49·2; H, 6·3; Te, 21·9. $C_{24}H_{37}O_3BrTe$ requires C, 49·6; H, 6·3; Te, 22·0%).

Ethyl and *l*-menthyl *n*-butyltelluroacetate each combined with an equimolecular proportion of methyl iodide; the products did not crystallise.

l-*Menthyl Tellurodiacetate*.—After removal of *l*-menthyl *n*-butyltelluroacetate from the decomposition products of the *l*-menthyl ester of di-*n*-butyltelluretine bromide (40 g.), the residue was dissolved in ether, and the solution filtered from deposited tellurium and concentrated. The yellow crystals which separated, recrystallised from methyl alcohol, yielded l-*menthyl tellurodiacetate* (11 g.), m. p. 58°, $[\alpha]_{5461}^{15°}$ − 27·6° in ether (*l*, 2; *c*, 1·25), $[\alpha]_{5461}^{17·5°}$ − 34·4° in chloroform (*l*, 2; *c*, 1·25), soluble in all the common organic solvents (Found: C, 54·5; H, 7·9; Te, 25·4; equiv., 264. $C_{24}H_{42}O_4Te$ requires C, 55·3; H, 8·1; Te, 24·5%; equiv., 259).

*Oxidation of Di*-n-*butyl Telluride*.—(i) *By atmospheric oxygen*. The amorphous white *solid* (II) (3·2 g.) which was deposited from di-*n*-butyl telluride (25 g.) on exposure to air during 6 months decomposed at 180° and was very sparingly soluble in ethyl alcohol and in benzene (Found: C, 25·3; H, 5·3; Te, 55·8; equiv., 313. $C_{20}H_{48}O_7Te_4$ requires C, 26·4; H, 5·3; Te, 56·0%; equiv., 304).

(ii) *By hydrogen peroxide*. To a cooled solution of di-*n*-butyl telluride (5·8 g., 1 mol.) in acetone (15 c.c.), hydrogen peroxide (30%) was added until precipitation ceased. The white *solid* (VI) obtained (3 g.) was washed with water and dried in a vacuum. It decomposed at 180°, was sparingly soluble in acetone and in benzene, and readily soluble in hot ethyl alcohol, giving a solution which gelatinised on cooling (Found: C, 33·4; H, 6·3; Te, 52·1; equiv., 721. $C_{20}H_{46}O_4Te_3$ requires C, 32·8; H, 6·3; Te, 52·2%; equiv., 732). After removal of a second crop which separated (0·5 g.) (Found: C, 32·8; H, 6·4; Te, 52·0%), the mother-liquor was made alkaline, concentrated, acidified with sulphuric acid, and distilled (bath temp. 200°). The distillate, which had the smell of butyric acid, was neutralised (phenolphthalein) with aqueous calcium hydroxide and evaporated to dryness. The residue of calcium butyrate decomposed at 150° and was analysed by ignition with sulphuric acid (Found: Ca, 18·8. Calc. for $C_8H_4O_4Ca$: Ca, 18·7%).

(iii) *By alkaline hydrogen peroxide*. A solution of hydrogen peroxide (50 c.c. of 20%; 16 mols.) and potassium hydroxide (5 g., 4 mols.) in water (100 c.c.) was added slowly to di-*n*-butyl telluride (4·7 g., 1 mol.) in acetone (50 c.c.). The oil which separated solidified on cooling and was recrystallised from ethyl alcohol. The *di*-n-*butyltelluronium dihydroxide* (VIII) (3·5 g.) obtained, soluble only in acetone, lost water at 120° and the residue decomposed at 175° (Found: C, 34·5; H, 7·0; Te, 45·9. $C_8H_{20}O_2Te$ requires C, 34·9; H, 7·3; Te, 46·3%).

(iv) *By nitric acid*. The oil which separated when di-*n*-butyl telluride (5 g.) was refluxed with excess of dilute nitric acid solidified on cooling to a mass of colourless crystals of *di*-n-*butyltelluronium hydroxy-nitrate* (X) (5 g.), m. p. 84°, which was soluble in the common organic solvents, was decomposed to a white amorphous solid by water, and exploded at 120°/20 mm. (Fond: C, 31·0; H, 5·7; Te, 40·1; equiv., 315. $C_8H_{19}O_4NTe$ requires C, 30·0; H, 6·0; Te, 39·8%; equiv., 320).

*Oxidation of Ethyl* n-*Butyltelluroacetate*.—(i) *By atmospheric oxygen*. The white *solid* (III) (1·2 g.) which separated from ethyl *n*-butyltelluroacetate (5 g.) on exposure to air during 2 months was washed with light petroleum and dried in a vacuum. It decomposed without melting

at 180° and was soluble only in warm ethyl alcohol (Found: C, 25·3; H, 4·5; Te, 52·5; equiv., 250. $C_{16}H_{36}O_7Te_2$ requires C, 26·6; H, 5·0; Te, 53·0%; equiv., 241).

(ii) *By hydrogen peroxide.* Hydrogen peroxide (30%) was added to the ethyl ester, in acetone solution, until precipitation ceased. The amorphous white precipitate (III) had the same properties as that described in (i) (Found: C, 25·9; H, 5·2; Te, 53·7%; equiv., 245).

*Oxidation of* l-*Menthyl* n-*Butyltelluroacetate*.—(i) *By atmospheric oxygen.* n-*Butyltellurinic acid* (I) (1·4 g.) separated as a white solid from *l*-menthyl *n*-butyltelluroacetate (15 g.) on exposure to air during 8 months [Found: C, 22·8; H, 4·2; Te, 58·4; equiv. (determined as described on p. 344, but without refluxing), 217. $C_4H_{10}O_2Te$ requires C, 22·1; H, 4·6; Te, 58·6%; equiv., 213]. The acid decomposed at 250°, was sparingly soluble in warm ethyl alcohol, soluble with decomposition in carbon disulphide and in acetic acid, insoluble in cold 3N-aqueous potassium hydroxide, soluble in hot N-alcoholic potassium hydroxide, and decomposed by hot water, giving an alkaline solution (possibly of *n*-butyltelluronium trihydroxide) and an insoluble residue.

(ii) *With hyperol* (*urea perhydrate*). A solution of hyperol (0·4 g., 1 mol.) in ethyl alcohol (20 c.c.) was added to the *l*-menthyl ester (1·5 g., 1 mol.), with cooling. *n*-Butyltellurinic acid (0·25 g.), identical in properties with that described in (i) above, separated from the solution during 2 days (Found: C, 22·7; H, 4·3; Te, 58·2%; equiv., 216).

(iii) *By hydrogen peroxide.* Hydrogen peroxide (30%) was added to the *l*-menthyl ester (10 g.) in acetone solution (25 c.c.), until precipitation ceased. The *precipitate* (V) was separated, washed with water and with acetone, and dried in a vacuum (Found: C, 39·3; H, 6·4; Te, 41·8; equiv., 184. $C_{14}H_{40}O_6Te_2$ requires C, 39·1; H, 6·5; Te, 41·7%; equiv., 182). The substance decomposed at 220°, was soluble in chloroform, carbon disulphide, and pyridine, and slightly soluble in warm water, giving an alkaline solution. It lost weight (approx. 40%) on trituration with N-sodium carbonate; the alkaline extract contained tellurium but gave no precipitate on acidification, and the residue, which decomposed at 150°, was insoluble in all solvents.

The substance (V) (5 g.) on trituration with cold 3N-nitric acid was converted into a *substance* (VII), which decomposed with effervescence at 130°, was insoluble in organic solvents, but soluble in hot N-potassium hydroxide with liberation of menthol (Found: C, 36·5; H, 5·7; Te, 38·3; equiv., 210. $C_{20}H_{39}O_7NTe_2$ requires C, 36·4; H, 6·0; Te, 38·7%; equiv., 220). Trituration of (VII) with N-sodium carbonate left a residue insoluble in all solvents, the composition of which was not elucidated (Found: C, 33·0; H, 5·0; Te, 41·0%).

On addition of aqueous ammonia to the nitric acid washings separated in the preparation of (VII), an amorphous white precipitate (probably impure tellurium dioxide) was obtained (Found: C, 5·8; H, 1·0; Te, 77·7. Calc. for $TeO_2$: Te, 79·9%. A second preparation gave C, 4·6; H, 1·4; Te, 74·6%).

(iv) *By nitric acid.* From a mixture of *l*-menthyl *n*-butyltelluroacetate (5 g., 1 mol.) and 6N-nitric acid (100 c.c., 5 mols.) the *hydroxy-nitrate* of *l*-menthyl *n*-butyltelluroacetate (XI) (6 g.) separated as a glassy solid. After being washed with water and dried in a vacuum, it had m. p. 42° (decomp. with efferv. at 140°) and was soluble in acetone, ethyl alcohol and ether, insoluble in other solvents and in water (Found: C, 42·5; H, 6·7; Te, 27·0; equiv., 223. $C_{15}H_{31}O_6NTe$ requires C, 41·7; H, 6·7; Te, 27·7%; equiv., 229). When heated at 100°/20 mm. for 1 hour, the hydroxy-nitrate lost weight (approx. 5%).

From a mixture of the hydroxy-nitrate (5 g., 1 mol.) and diethylamine (0·9 g., 1 mol.) in ether (50 c.c.) a white solid (3 g.) separated, which decomposed at 203° and was soluble in 6N-potassium hydroxide with liberation of menthol. On trituration of this product with water, diethylamine nitrate passed into solution; the insoluble *residue* (IV) decomposed at 210° (Found: C, 24·4; H, 4·6; Te, 55·1. $C_{14}H_{32}O_7Te_3$ requires C, 24·2; H, 4·6; Te, 55·1%).

From a mixture of equimolecular proportions of the hydroxy-nitrate and aniline in dry ether, aniline nitrate separated; a solid product could not be isolated from the filtered etherea solution.

(v) *By benzoyl peroxide.* Benzoyl peroxide (2·4 g., 1 mol.) in chloroform (25 c.c.) was addec to the *l*-menthyl ester (3·8 g., 1 mol.) in chloroform (25 c.c.). The mixture, which becam warm, was heated under reflux for 1 hour, and the chloroform allowed to evaporate at roon temperature. After 4 days, the deposited *dibenzoate of l*-menthyl *n*-butyltelluroacetate dihydr oxide (IX) (5·4 g.) was removed, washed with water, and dried in a vacuum. It was soluble i ethyl alcohol, insoluble in water and in light petroleum (Found: C, 57·2; H, 6·7; Te, 19·8 $C_{30}H_{40}O_6Te$ requires C, 57·7; H, 6·5; Te, 20·4%).

*Di-*n-*butyltelluronium Di-iodide and* n-*Butyltelluronium Tri-iodide*.—(i) *From di-*n-*but*

*telluride.* On evaporation at room temperature of a mixture of di-*n*-butyl telluride (2·4 g., 1 mol.) and iodine (2·6 g., 1 mol.) in carbon tetrachloride (50 c.c.), there was deposited a mixture of red crystals (3·5 g.), soluble in light petroleum, and a blue-black micro-crystalline powder, insoluble in light petroleum. The red crystals, recrystallised from light petroleum, gave *di*-n-*butyltelluronium di-iodide*, m. p. 61°, soluble in the common organic solvents, sparingly soluble in water (Found : C, 19·5; H, 3·6; I, 51·5; Te, 25·8; equiv., 245. $C_8H_{18}I_2Te$ requires C, 19·4; H, 3·6; I, 51·3; Te, 25·7%; equiv., 247). The blue-black powder was washed with light petroleum, leaving n-*butyltelluronium tri-iodide* (Found : C, 8·4; H, 1·9; I, 67·5; Te, 22·9. $C_4H_9I_3Te$ requires C, 8·5; H, 1·6; I, 67·3; Te, 22·6%), which was soluble in acetone and in ethyl alcohol and decomposed on heating, with liberation of iodine.

The di-iodide was recovered unchanged after trituration with hydriodic acid. On addition of hydriodic acid to the di-iodide in acetone solution, followed by evaporation of the acetone at room temperature, crystals of the tri-iodide were deposited.

(ii) *From di*-n-*butyltelluronium dihydroxide.* Hydriodic acid (10 c.c. of 50%; 2 mols.) was added slowly to the dihydroxide (2·8 g., 1 mol.), suspended in acetone (25 c.c.), and the resulting clear red solution was extracted with light petroleum. The extract, washed with water, dried (sodium sulphate), and concentrated at room temperature, deposited orange crystals of di-*n*-butyltelluronium di-iodide, m. p. 61°. The extracted solution, on evaporation, deposited *n*-butyltelluronium tri-iodide, which after recrystallisation from acetone was identical in properties with that described in (i) above.

(iii) *From* (II), (III), *and* (VI). Hydriodic acid (10 c.c. of 57%) was added to each of these compounds (3·2 g.), suspended in acetone (20 c.c.). The resulting di-iodide (Found : C, 19·0; H, 3·7; Te, 24·8%) and tri-iodide (Found : Te, 22·9%) were isolated as described in (ii) above.

(iv) *From ethyl* n-*butyltelluroacetate.* Iodine (2·5 g., 1 mol.) in ether (50 c.c.) was added slowly to the ethyl ester (2·7 g., 1 mol.) in ether (10 c.c.). The solution was evaporated at room temperature to 10 c.c. and extracted with light petroleum. The di-iodide, m. p. 60° (Found : C, 19·7; H, 3·8; Te, 25·1%), and tri-iodide (Found : C, 8·4 : H, 2·0; Te, 22·5%) were isolated as described in (i) above. The fluid by-products had the characteristic smell and lachrymatory effect of ethyl iodoacetate.

*Oxidation of* l-*Menthyl Tellurodiacetate.*—Addition of hydrogen peroxide (30%) to the *l*-menthyl ester in acetone solution precipitated a white solid, which was washed with water and with acetone and recrystallised from aqueous alcohol. The *hydroxy-perhydrate* of *l*-menthyl tellurodiacetate obtained had m. p. 90° (decomp. with efferv. at 145°) (Found : C, 50·9; H, 7·5; Te, 24·5. $C_{24}H_{44}O_7Te$ requires C, 50·5; H, 7·7; Te, 22·3%). It was soluble in ether, light petroleum, acetic acid, and alcohol, insoluble in water and in acetone. In acetic acid solution the hydroxy-perhydrate liberated iodine from potassium iodide and bromine from hydrobromic acid and rapidly decolorised aqueous potassium permanganate.

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BATTERSEA POLYTECHNIC, LONDON, S.W. 11. [*Received, December 21st, 1937.*]

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## 70. *Condensation Products of Phenols and Ketones. Part II. Catechol and Acetone.**

By WILSON BAKER and JOHN C. MCGOWAN.

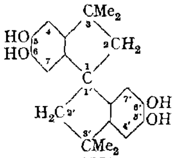
A condensation product of catechol and acetone, $C_{21}H_{24}O_4$, has been proved to be 5 : 6 : 5′ : 6′-tetrahydroxy-3 : 3 : 3′ : 3′-tetramethylbis-1 : 1′-*spiro*hydrindene as was suggested by one of the authors in 1934. The structure as a bis-1 : 1′-*spiro*hydrindene was established by oxidation with potassium permanganate, phoronic anhydride, $C_{11}H_{16}O_4$, being isolated. Aerial oxidation in alkaline solution led to the opening of both catechol nuclei and formation of a tetracarboxylic acid without loss of carbon atoms; this acid on reduction and decarboxylation yielded a bis-*spirocyclo*pentene, $C_{17}H_{28}$, whose properties are consistent only with the given positions of the hydroxyl groups in the original compound.

* The paper by Baker entitled "The Condensation of Catechol with Acetone" (J., 1934, 1678) is to be regarded as Part I of the series.

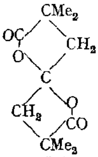
CATECHOL condenses with acetone in presence of acetic and hydrochloric acids to form a compound $C_{21}H_{24}O_4$ (I), which is equivalent to $2C_6H_4(OH)_2 + 3C_3H_6O - 3H_2O$. This substance was first prepared by Fabinyi and Széky (*Ber.*, 1905, **38**, 2307), who suggested the improbable structure $(HO)_2C_6H(CMe_2)_3C_6H(OH)_2$ (II), which, as pointed out by Ghiglieno (*Atti R. Accad. Sci. Torino*, 1912, **47**, 16), does not account for the ready formation of a tetrabromo-derivative on treatment with bromine in acetic acid. Ghiglieno showed that the compound could be produced equally easily when catechol was condensed, not with acetone, but with the equivalent amount of phorone (compare Baker, *loc. cit.*), and he suggested the structure $[(HO)_2C_6H_3]_2C(CH{:}CMe_2)_2$. This, however, cannot be correct, because, as pointed out by Fisher, Furlong, and Grant (*J. Amer. Chem. Soc.*, 1936, **58**, 820), such a compound would yield a polybromo-derivative containing more than four atoms of bromine, and would show the unsaturation characteristic of ethylenic compounds. We have been unable to reduce (I) or its tetramethyl ether by catalytic methods, and similar negative results under more drastic conditions have been recorded by Remesat (Dissert., Berlin, 1930, "Versuchung über die Kondensation von Brenzkatechin und Guajacol mit Aldehyden und Ketonen"). Remesat also carried out a number of high-temperature but uninformative degradations of (I) which threw no new light on its structure, and he retained the original formula (II).

Sükösd (*Acta Lit. Sci. Univ. Hung. Francisco-Josephinae*, 1932, 2, 230; *Amer. Chem. Abs.*, 1933, **27**, 1873) obtained a condensation product of guaiacol and acetone and suggested for it a structure analogous to (II). Fisher, Furlong, and Grant (*loc. cit.*), however, have shown that the dimethyl ether of Sükösd's compound is identical with the tetramethyl ether of (I), so that the objections to (II) apply equally to the guaiacol-acetone compound.

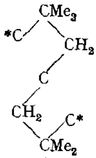
The condensation product, $C_{21}H_{24}O_4$ (I), of catechol and acetone was reinvestigated in 1934 (Baker, *loc. cit.*), and the suggestion was made that it was probably 5 : 6 : 5′ : 6′-tetrahydroxy-3 : 3 : 3′ : 3′-tetramethylbis-1 : 1′-*spiro*hydrindene (III), on the following grounds. (1) It contains four phenolic groups, yielding a tetra-acetate, tetrabenzoate, and tetramethyl ether, and a double ortho-quinone reducible to the original compound; (2) four hydrogen atoms and four only are instantaneously replaced by bromine on treatment with bromine in acetic acid; most probably this involves two hydrogen atoms in each of the catechol nuclei; (3) it contains no ethylenic bonds; (4) phorone is an intermediate in its formation. With regard to (2) it has now been found that under the same conditions 5 : 6-dihydroxyhydrindene readily yields 4 : 7-*dibromo*-5 : 6-*dihydroxyhydrindene*.



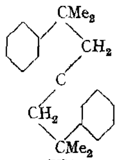
(III.)



(IV.)



(V.)



(VI.)

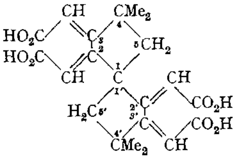
Although the structure (III) appeared to be the only one consistent with the then known facts and has been accepted by recent workers (Fisher, Furlong, and Grant), there was little direct proof of its accuracy, but the experiments now recorded prove that the substance is a tetrahydroxy-3 : 3 : 3′ : 3′-tetramethylbis-1 : 1′-*spiro*hydrindene of the type (III), the only point not established with *absolute* rigidity being the positions of the hydroxy groups, although no reasonable doubt can be entertained that they occupy positions 5, 6, 5′ and 6′ as in (III).

Oxidation of (I) with potassium permanganate and treatment of the product wit[h] acetic anhydride led to the isolation in small yield of phoronic anhydride (IV). Phoroni[c] anhydride was also obtained similarly from the carefully purified tetra-acetate of (I[).] This established the presence in the compound of the grouping (V). It is clear that, [...]

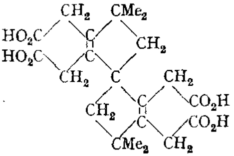
the nine carbon atoms in the grouping $\cdot CMe_2\cdot CH_2\cdot C\cdot CH_2\cdot CMe_2\cdot$, none could have formed part of an aromatic nucleus, and these nine carbon atoms therefore represent the three molecules of acetone involved in the condensation, and it is to be noted that they are combined as in phorone. The two remaining carbon atoms marked with asterisks in (V) must, therefore, have formed part of the two catechol nuclei,* so that the structure may be expanded to (VI). Of the remaining eight hydrogen atoms not shown in (VI), four are present in hydroxyl groups, and four as nuclear hydrogen atoms (because the compound yields a tetrabromo-derivative), so that the central carbon atom, which becomes a carbonyl group during oxidation, must be quaternary, and this can only be achieved by *its being united to the two aromatic nuclei in two positions ortho to the* $CMe_2$ *groups*, as in (III). For stereochemical reasons it is clearly impossible that the central carbon atom in (VI) could be united to the aromatic nuclei in the positions meta or para to the $CMe_2$ groups.

With regard to the hydroxyl groups it is almost certain from a consideration of the general activity of catechol and of guaiacol, which gives a product with the same orientation, that these occupy positions 5, 6, 5′, and 6′ as in (III). Evidence from the great stability of the corresponding *o*-quinone (Baker, *loc. cit.*; Fisher, Furlong, and Grant, *loc. cit.*) is of no value, because we have now found that 5 : 6-*hydrindenequinone* is not more stable or more readily formed than *o*-benzoquinone itself. Again, arguments based on coupling experiments in the case of the guaiacol condensation product (Fisher, Furlong, and Grant) are inconclusive, and, in view of the note of Fieser and Lothrop (*J. Amer. Chem. Soc.*, 1937, **59**, 945), are of very doubtful value. Evidence very strongly supporting the structure (III) has now been obtained from a study of the properties of another oxidation product of the compound $C_{21}H_{24}O_4$ (I).

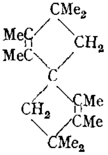
Aerial oxidation of (I) in aqueous alkaline solution results in the absorption of four atoms of oxygen and formation of a tetracarboxylic acid, $C_{17}H_{20}(CO_2H)_4$, which, if the hydroxyl groups occupy the positions shown in (III), must be 2 : 3 : 2′ : 3′-*tetra(carboxymethylene)*-4 : 4 : 4′ : 4′-*tetramethylbis*-1 : 1′-spirocyclo*pentane* (VII). This acid (VII)



(VII.)



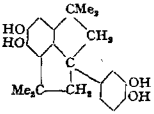
(VIII.)



(IX.)

yields phoronic acid, isolated as its anhydride, when oxidised with potassium permanganate, and, when reduced with sodium amalgam, takes up two molecules of hydrogen, giving 4 : 4 : 4′ : 4′-*tetramethylbis*-1 : 1′-spirocyclo*pentene*-2 : 3 : 2′ : 3′-*tetra-acetic acid* (VIII), this partial reduction with sodium amalgam being characteristic of muconic acid and derivatives. *Methyl* and *ethyl* esters of (VIII) were prepared. The calcium and barium salts

* It should be pointed out for the sake of completeness that these two carbon atoms could not have been ortho- or para-carbon atoms of one catechol nucleus, since the former would require a 7- and a 3-membered ring fused one to each of the two aromatic nuclei, and the latter a chain of five carbon atoms connecting the para-positions of one nucleus and a 3-membered ring fused to the other. If, however, they were two meta-carbon atoms of one nucleus, this would lead to the structure annexed. Apart from its intrinsic improbability a compound of such structure could not be expected to yield a double ortho-quinone on oxidation with fuming nitric acid in alcohol, nor could it give any satisfactory explanation for the formation of the acids $C_{21}H_{24}O_8$ and $C_{21}H_{22}O_8$ or the hydrocarbon $C_{17}H_{28}$, here represented by the formulæ (VII), (VIII), and (IX), which clearly involves two symmetrically placed catechol nuclei.



of (VII) and (VIII) are much more soluble in cold than in hot water. When heated, the acid (VIII) readily loses four molecules of carbon dioxide, yielding a hydrocarbon $C_{17}H_{28}$, 2 : 3 : 4 : 4 : 2′ : 3′ : 4′ : 4′-*octamethylbis*-1 : 1′-spirocyclo*pentene* (IX). This hydrocarbon readily combines with four atoms of bromine in acetic acid solution, but does not undergo catalytic reduction with hydrogen in presence of either palladium chloride, palladium deposited on strontium carbonate, or Adams's platinum oxide catalyst under three atmospheres pressure. This failure to reduce gives very strong support to the structure (IX), and hence to the structure (III) for the original condensation product, since owing to the methyl groups attached to the double bonds in (IX), and the quaternary nature of the adjacent carbon atoms 1, 4, and 4′, resistance to reduction might well be expected. If, however, the hydroxyls in the condensation product occupied either positions 4, 5, 4′, and 5′ or positions 6, 7, 6′, and 7′, then the hydrocarbon $C_{17}H_{28}$ would contain two ethylidene groups, $CH_3\cdot CH\colon$, and no resistance to reduction could be expected. The simultaneous loss of four molecules of carbon dioxide from (VIII) also indicates that the carboxyl groups are all very similarly placed in the molecule, which would not be the case if (VIII) were derived from catechol–acetone condensation products possessing either of the two alternative arrangements of the hydroxyl groups. Further, if the hydroxyls occupied positions 6, 7, 6′, and 7′, then the acid corresponding to (VIII) would have carboxyl groups united to carbon atoms 2 and 2′ and would be a glutaric acid derivative; as such it would be expected that these two carboxyl groups would yield an anhydride on heating instead of losing carbon dioxide.

Many unsuccessful attempts have been made to degrade the very stable tetramethyl ether of (III) to *m*-hemipinic acid, and thus to establish the positions of the methoxyl groups. Among the recorded conditions are treatment with potassium permanganate in acetone and pyridine solution (Remesat, Baker), and with chromic anhydride in acetic acid (Fisher, Furlong, and Grant). Fusion with caustic alkalis under a variety of conditions, both with and without the addition of oxidising agents, has also given negative results. Attempts to resolve the guaiacol–acetone condensation product by means of its di-*l*-menthoxyacetate were unsuccessful, the ester being obtained only as a non-crystalline resin.

A crystallographical examination of the dimorphic forms of the tetramethyl ether of (III) (see Part I) was kindly undertaken by Mr. H. M. Powell of the Department of Mineralogy, University Museum, Oxford, who reports as follows :—

"Crystals of the β modification belong to the anorthic system and develop the forms {100} {010} {001} {110} {$\bar{1}$10} {201} {$\bar{2}$01}. From measurements of interfacial angles on the goniometer the crystallographic constants are calculated to be $a : b : c = 1{\cdot}408 : 1 : 0{\cdot}5578$; $\alpha = 108° 46'$, $\beta = 103° 51'$, $\gamma = 82° 12'$. Etch figures and the absence of pyroelectric effect show that the crystals have a centre of symmetry. *X*-Ray photographs obtained with copper radiation give the unit cell dimensions as $a_0 = 21{\cdot}64$, $b_0 = 14{\cdot}35$, $c_0 = 7{\cdot}99$ A. The density was found to be 1·15 g./c.c. and hence the number of molecules per unit cell is $4{\cdot}02 \approx 4$.

"The α-form is tetragonal. The crystals are badly formed bipyramids and are optically uniaxial. Oscillation photographs obtained with copper radiation show that there is a pseudo-cell of dimensions $a_0 = 8{\cdot}40$, $c_0 = 33{\cdot}0$ A. The density was found to be 1·11 g./c.c. and the calculated number of molecules per unit cell is $3{\cdot}96 \approx 4$. Very faint intermediate layer lines obtained on oscillation about the *a* axis show, however, that the true *a* dimension is four times that of the pseudo-cell and hence indicate a cell sixteen times this size.

"For both modifications the cell size and density therefore give a molecular weight in agreement with the proposed formula for this substance, and models constructed for the purpose show that the molecules may be packed into the space available."

The elucidation of the structure of other condensation products of acetone and phenols along the lines described in this paper is in progress. It has already been established that both hydroxyquinol and *m*-cresol yield derivatives of 4 : 4 : 4′ : 4′-tetramethylbis-2 : 2′-*spiro*chroman, but that pyrogallol gives a 3 : 3 : 3′ : 3′-tetramethylbis-1 : 1′-*spiro*hydrindene.

EXPERIMENTAL.

*Oxidation of the Compound* $C_{21}H_{24}O_4$ *and Isolation of Phoronic Anhydride* (IV).—5 : 6 : 5′ : 6′-Tetrahydroxy-3 : 3 : 3′ : 3′-tetramethylbis-1 : 1′-*spiro*hydrindene (III) (10 g.) was finely powdered, and a warm saturated aqueous solution of potassium permanganate slowly added with constant agitation, until the colour of the solution indicated that it was present in considerable excess; the mixture was then kept overnight. After passage of excess of sulphur dioxide the liquid was extracted with ether, and the extract dried over sodium sulphate and distilled, leaving a somewhat rancid-smelling liquid (4·5 g.); this contained acetic acid, and, judging by the odour, possibly also *iso*butyric and *iso*valeric acids.* This was refluxed with acetic anhydride (10 c.c.) for 1 hour, and, after shaking with water, was submitted to steam distillation. The distillate yielded to ether an oil which solidified in contact with water; the solid (about 0·5 g.) was collected, washed with cold dilute sodium hydroxide solution and water, dried, and crystallised first from light petroleum (b. p. 60—80°), and then twice from light petroleum (b. p. 80—100°). The phoronic anhydride separated in long flat prisms, m. p. 128—129° (Found : C, 62·4; H, 7·6; *M*, 220. Calc. for $C_{11}H_{16}O_4$ : C, 62·3; H, 7·5%; *M*, 212).

Phoronic anhydride was also obtained by the oxidation of pure 5 : 6 : 5′ : 6′-tetra-acetoxy-3 : 3 : 3′ : 3′-tetramethylbis-1 : 1′-*spiro*hydrindene, m. p. 174—175°, which had been twice crystallised from alcohol, and submitted to a preliminary hydrolysis with a little alcoholic potassium hydroxide, the alcohol being removed before the addition of the permanganate.

A specimen of phoronic anhydride was synthesised by the action of acetic anhydride on phoronic acid (Pinner, *Ber.*, 1881, **14**, 1070). After crystallising twice from light petroleum, (b. p. 80—100°) it had m. p. 128·5—129·5°, undepressed on admixture with the anhydride previously prepared. All specimens were identical in their crystalline habit.

*Oxidation of the Compound* $C_{21}H_{24}O_4$ *and Isolation of* 2 : 3 : 2′ : 3′-*Tetra*(*carboxymethylene*)-4 : 4 : 4′ : 4′-*tetramethylbis*-1 : 1′-spirocyclo*pentane* (VII).—5 : 6 : 5′ : 6′-Tetrahydroxy-3 : 3 : 3′ : 3′-tetramethylbis-1 : 1′-*spiro*hydrindene (III) (10 g.), dissolved in a solution of sodium hydroxide (40 g.) in water (300 c.c.), was oxidised by bubbling air through the solution for 50 hours, a layer of light petroleum (b. p. 100—120°) being floated on the solution to prevent frothing. Ether (100 c.c.) was now added to the solution, which was cooled and stirred during the addition of excess of hydrochloric acid. A pale yellow, crystalline powder separated and a small amount of resinous material was taken up by the ether. After an hour the product was collected and washed thoroughly with water and ether (yield, 8·9 g.; 75% of the theoretical). For analysis it was crystallised three times from 50% aqueous acetic acid, and dried in a vacuum over potassium hydroxide at 100°, being obtained as a very pale yellow, microcrystalline powder, m. p. about 260° with evolution of carbon dioxide [Found : C, 62·1; H, 5·9; equiv., by titration with cold sodium hydroxide solution and phenolphthalein, 100·7. $C_{17}H_{20}(CO_2H)_4$ requires C, 62·4; H, 5·9%; equiv., 101].

2 : 3 : 2′ : 3′-*Tetra*(*carboxymethylene*)-4 : 4 : 4′ : 4′-*tetramethylbis*-1 : 1′-spirocyclo*pentane* is very sparingly soluble in hot water, ether, acetone, and ethyl acetate, but soluble in alcohol and acetic acid. It does not react with bromine in acetic acid, and is apparently unaltered by boiling with excess of acetic anhydride for 10 hours. The barium salt was prepared by heating a solution of the acid in the minimum quantity of dilute aqueous ammonia with excess of barium acetate, collecting the precipitate at the boiling point, and washing it with boiling water. This salt is easily soluble in cold water, but very sparingly soluble in hot water. When oxidised with potassium permanganate solution as described under the similar oxidation of the condensation product (III), the acid ultimately yielded phoronic anhydride, m. p. 126—127° (the mixed m. p. with the synthetical anhydride, m. p. 128·5—129·5°, was 128—129°). The product obtained by heating the acid above its m. p. was mainly resinous, but a small quantity of a yellow volatile hydrocarbon possessing a powerful terpene-like odour was isolated by steam distillation.

4 : 4 : 4′ : 4′-*Tetramethylbis*-1 : 1′-spirocyclo*pentene*-2 : 3 : 2′ : 3′-*tetra-acetic Acid* (VIII).—2 : 3 : 2′ : 3′-Tetra(carboxymethylene)-4 : 4 : 4′ : 4′-tetramethylbis-1 : 1′-*spirocyclo*pentane (VII) (20 g.), suspended in water (400 c.c.), was heated on a steam-bath, and 4% sodium amalgam added at intervals with occasional stirring until reduction was complete (about 8 hours). The solution was cooled, filtered, and acidified with hydrochloric acid, and the solid precipitate

* On several occasions this liquid became pasty with crystals of phoronic anhydride after a few hours. The spontaneous deposition of the anhydride, however, could not be relied upon, and it was found convenient to treat the product with acetic anhydride.

collected after an hour and washed thoroughly with water. It was recrystallised twice from aqueous alcohol, being obtained in minute hexagonal plates, m. p. about 260° (decomp.) (yield, almost quantitative) [Found: C, 61·4; H, 6·7; equiv. by titration with cold sodium hydroxide solution and phenolphthalein, 104·1. $C_{17}H_{24}(CO_2H)_4$ requires C, 61·8; H, 6·8%; equiv., 102]. This acid is oxidised by a warm solution of potassium permanganate but does not decolourise a solution of bromine in acetic acid. The calcium salt was prepared by boiling a solution of the sodium salt with a solution of calcium acetate; it was collected while hot and washed with boiling water. This salt is much more soluble in cold water than hot; 100 g. of water dissolve 14·2 g. at 15°, but only 0·57 g. at 100° (compare calcium citrate); the cold aqueous solution is rather viscous and froths easily. No smooth decomposition takes place on distillation of the calcium salt and no ketone appears to be produced.

The *tetramethyl* ester of this acid was prepared by refluxing a solution of the acid in ten times its weight of absolute methyl alcohol containing anhydrous hydrogen chloride for 8 hours. After the addition of excess of sodium bicarbonate solution the ester was extracted with ether, and the ethereal solution dried and distilled. The residual ester was distilled twice under diminished pressure, and the middle fraction collected in each case. It formed an odourless, pale yellow oil, b. p. 195°/0·36 mm., 202°/0·53 mm. (Found: C, 64·6; H, 7·9; *M*, 437. $C_{25}H_{36}O_8$ requires C, 64·6; H, 7·8%; *M*, 464). The *tetra-ethyl* ester, obtained in the same way, formed an odourless, pale yellow oil, b. p. 243°/2 mm. (Found: C, 66·5; H, 8·6; *M*, 528. $C_{29}H_{44}O_8$ requires C, 66·9; H, 8·5%; *M*, 520).

2 : 3 : 4 : 4 : 2′ : 3′ : 4′ : 4′-*Octamethylbis*-1 : 1′-spirocyclo*pentene* (IX).—4 : 4 : 4′ : 4′-Tetramethylbis-1 : 1′-*spirocyclo*pentene-2 : 3 : 2′ : 3′-tetra-acetic acid (VIII) (20 g.) was heated in a small flask in portions of 5 g. until nothing further distilled. The product was submitted to steam-distillation, and the volatile oil (5·1 g.) extracted from the distillate with ether. It formed a colourless liquid, b. p. 130—131°/18 mm., 250°/760 mm. (Found: C, 88·0; H, 11·9. $C_{17}H_{28}$ requires C, 87·9; H, 12·1%), with a weak, rather fatty odour. It is soluble in most organic solvents, but does not mix completely with acetic acid. It yields no picrate or picrolonate.

As usually prepared, this hydrocarbon reacts with potassium permanganate in the cold, but when treated with hydrogen and a catalyst under any of the conditions described in the theoretical part of the paper it rapidly takes up about 1/6 mol. of hydrogen, and is not further reduced (complete reduction of $C_{17}H_{28}$ requires 2 mols. of hydrogen), but the product is then completely unattacked by potassium permanganate. This result is probably to be ascribed to a trace of the unreduced acid (VII) in the acid (VIII) from which the hydrocarbon is prepared. In spite of its reluctance to combine with hydrogen the hydrocarbon (IX) readily decolourises bromine water and a solution of bromine in acetic acid in the cold, and the amount of bromine taken up in the latter case proves the presence of two double bonds in the molecule. A solution of (IX) (treated with hydrogen and platinum oxide under 3 atms. for 4 hours) was titrated with a 10% solution of bromine in acetic acid, the final end-point being determined by an external starch–potassium iodide indicator; bromine corresponding to 1·96 mols. was absorbed for each molecule of hydrocarbon.

4 : 7 : 4′ : 7′-*Tetrabromo*-5 : 6 : 5′ : 6′-*tetramethoxy*-3 : 3 : 3′ : 3′-*tetramethylbis*-1 : 1′-spiro*hydrindene*.—4 : 7 : 4′ : 7′-Tetrabromo-5 : 6 : 5′ : 6′-tetrahydroxy-3 : 3 : 3′ : 3′-tetramethylbis-1 : 1′-*spiro*hydrindene (4 g.) (Baker, *loc. cit.*) in methyl alcohol (7 c.c.) was treated alternately with excess of methyl sulphate and 20% aqueous potassium hydroxide, the mixture being allowed to boil. The solid *product* was collected, washed with dilute alkali solution and water, and crystallised twice from alcohol, forming microscopic needles, m. p. 205° (Found: Br, 45·0. $C_{25}H_{28}O_4Br_4$ requires Br, 44·9%).

5 : 6-*Dihydroxyhydrindene*.—5 : 6-Dimethoxyhydrindene (12 g.), glacial acetic acid (100 c.c.), and hydrobromic acid (100 c.c.; *d* 1·5) were refluxed for 6 hours. After dilution with a large volume of water, the dihydroxy-compound was extracted with ether, and the extracts shaken with excess of sodium bicarbonate solution and distilled, leaving a crystalline mass of a hydrate (10·5 g.), m. p., after drying at 100° in a vacuum over calcium chloride, 114—115° (cf. Mills and Nixon, J., 1930, 2510).

4 : 7-*Dibromo*-5 : 6-*dihydroxyhydrindene*.—A solution of 5 : 6-dihydroxyhydrindene (1 g.) in acetic acid (8 c.c.) was treated with a solution of bromine (2·13 g.; 2 mols.) in acetic acid (2 c.c.). Instant bromination occurred, and after 24 hours the rhombic plates which had separated were collected, boiled with charcoal in dilute alcoholic solution, precipitated by water, dried, and crystallised from light petroleum. The *product* formed fine prisms, m. p. 95° with previous softening (Found: Br, 51·5. $C_9H_8O_2Br_2$ requires Br, 51·9%).

5 : 6-*Hydrindenequinone*.—To 5 : 6-dihydroxyhydrindene (1 g.) in dry ether (20 c.c.) were added anhydrous sodium sulphate (3 g.) and silver oxide (3 g.). The mixture became warm and was boiled for 1 minute; the liquid was filtered rapidly, and the residue washed with a little ether. Evaporation of the filtrate to about 1/3 of its volume led to the separation of the *quinone* in bright red needles, which were collected and placed in an evacuated desiccator. The quinone melted at about 87°, and the crystals turned dark in a few hours; it reacted immediately with water (Found : C, 71·9; H, 4·2. $C_9H_8O_2$ requires C, 72·9; H, 5·4%). The substance may be recrystallised from ether or dioxan, but the solutions are not very stable.

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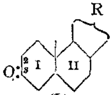
## 71. *The Action of Selenium Dioxide on Sterols and Bile Acids. Part IV. Cholestane-2 : 3-dione from Cholestan-3-one.*

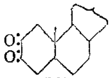
By E. T. STILLER and O. ROSENHEIM.

The action of selenium dioxide on unsaturated hydroxylated steroids leads in the first instance to α-glycols. By the oxidation of saturated and of unsaturated steroid ketones with the same reagent, α-diketones (diosphenols) have now been obtained. *Cholestane*-2 : 3-*dione* has been examined in detail and found to exist in two modifications, probably representing the tautomeric enolic forms of the diketone.

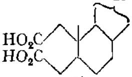
THE use of selenium dioxide as an oxidising agent in the steroid series, which has so far been applied only to unsaturated hydroxylated steroids (Callow and Rosenheim, J., 1933, 387; Callow, J., 1936, 462; Rosenheim and Starling, J., 1937, 377; cf. Butenandt and Hausmann, *Ber.*, 1937, **70**, 1154), has now been extended to saturated and unsaturated steroid ketones. Of the ketones examined, only cholestanone reacted readily in alcoholic solution. By analogy with the behaviour on bromination of the ketonic steroids belonging to the *trans*-series (Butenandt and Wolff, *Ber.*, 1935, **68**, 2091) it was to be expected that selenium dioxide would attack cholestanone (I) at the methylene group $C_2$ in ring I, introducing a carbonyl group. The reaction product, *cholestane*-2 : 3-*dione* (II), is a diosphenol and was readily separated from unchanged cholestanone by making use of the insolubility of its *potassium* salt in 20% aqueous potassium hydroxide and ether. The yield of the pure diosphenol was found to be dependent on the amount of the oxidising agent used and rose to a maximum of 30% when the proportion of cholestanone to selenium dioxide was 1 : 8 by weight. In spite of the large excess of oxidising agent a variable amount of unchanged cholestanone was recovered.



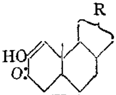
(I.)



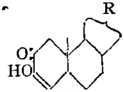
(II.)



(III.)



(IIa.)



(IIb.)

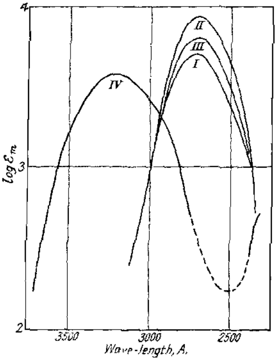
(R = $C_{16}H_{30}$)

The constitution of the diosphenol was established by the following evidence: The substance gives a purple colour with alcoholic ferric chloride and is further characterised as an α-diketone by its ready reaction in alcoholic solution with *o*-phenylenediamine,

yielding a ***quinoxaline*** derivative, m. p. 180°. As a diosphenol the diketone can exist in the mono-enol modification (II*a* or II*b*), and yields a ***monobenzoate*** and a ***monoacetate***, from which it is again obtained on hydrolysis. The position of the carbonyl groups at $C_2$ and $C_3$ was established by the quantitative oxidation with alkaline hydrogen peroxide to the dicarboxylic acid $C_{27}H_{46}O_4$ (III), previously obtained from cholestanone by oxidation with chromic acid (Windaus and Uibrig, *Ber.*, 1914, **47**, 2384).

The melting point (144—145°) of the diosphenol, regenerated from its potassium salt, remained unchanged after repeated crystallisations from different solvents. Some specimens, however, showed a surprising behaviour, the melting point occasionally falling to 130—132°, or rising to 156° or 168°, on further recrystallisation. An explanation for these perplexing changes was afforded by the observation that the substance occurred in two interconvertible modifications, form (A), m. p. 144—145°, and form (B), m. p. 168—169°. The two forms occur further as an equimolecular mixture (C), m. p. 130—132°.

*Absorption spectrum of cholestane-2 : 3-dione.*




(I), *Form* (A); (II), *form* (B); (III), [(A) + (B)]/2 = (C); (IV), (A), (B), *and* (C) *in alkaline solution.*

The interconversion of (A) and (B) can be brought about at will by means of mineral acids and alkalis. Thus, when form (A) is heated to 100° with glacial acetic acid containing a trace of hydrochloric acid, and the product recrystallised from ethyl acetate, form (B) is obtained. On the other hand, by converting form (B) into its enolic potassium salt and regenerating the diosphenol, form (A) is obtained. The dione, m. p. 130—132°, occasionally observed on recrystallisation of form (A), is also obtained on recrystallising together equivalent amounts of forms (A) and (B). From the following table it will be seen that the specific rotation, the rotatory dispersion $\alpha_{5461}/\alpha_D$, and log $\epsilon_m$ at 2700 A. (see figure) are those of an equimolecular mixture of forms (A) and (B) of the diosphenol.

| Form. | M. p. | $[\alpha]_{5461}$. | $[\alpha]_D$. | $\alpha_{5461}/\alpha_D$. | Log $\epsilon_m$ (2700 A.). |
|---|---|---|---|---|---|
| (A) | 144—145° | +91·5° | +79·1° | 1·16 | 3·70 |
| (B) | 168—169 | +67·3 | +57·2 | 1·18 | 3·93 |
| $\frac{(A) + (B)}{2}$ | 130—132 | +79·4 | +68·2 | 1·17 | 3·81 |
| (C) | 130—132 | +79·0 | +68·2 | 1·17 | 3·80 |

Forms (A) and (B), as well as the dione of m. p. 130—132°, yield the same quinoxaline derivative with *o*-phenylenediamine and the same dicarboxylic acid, $C_{27}H_{46}O_4$, on oxidation. The two forms give, however, different enolic monoacetates, m. p. 137—138° and 141—143° respectively, their mixture showing a depression of 30° in melting point. Both (A) and (B) give a purple ferric chloride reaction of the same intensity and a yellow colour with tetranitromethane, but differ characteristically in their colour reactions with concentrated sulphuric acid and other reagents.

The two substances are probably best regarded as the two tautomeric enolic forms (II*a* and II*b*) of the diosphenol, but it is not improbable that (A) is one of the enolic forms and (B) the diketone form which, in alcoholic solution, is in equilibrium with the other enolic form. Form (B) is evidently identical with the 2 : 3-diketone recently obtained in small yield by debromination of 2 : 4-dibromocholestanone by Inhoffen (*Ber.*, 1937, **70**, 1695). The variations in melting point and optical activity observed by this author may have been due to slight admixtures of form (A) of the diosphenol in his preparations.

The preparation of ***hydroxymethylenecholestan-3-one***, the oxidation of which offers another approach to cholestane-2 : 3-dione, is described.

## Experimental.

The reactivities of the various steroid ketones with selenium dioxide were tested as previously described (Callow and Rosenheim, J., 1933, 387). The following results were obtained:

(1) Cholestanone reacted readily and coprostanone slightly in alcoholic solution.

(2) The following ketones did not react in alcohol, but reacted readily in glacial acetic acid at 100°: $\Delta^4$-cholesten-3-one, cholestan-3-ol-6-one, cholestan-6-one, cholestane-3 : 6-dione, $\Delta^4$-cholestene-3 : 6-dione, 3 : 12-diketocholanic acid.

(3) Cholestan-3-ol-7-one acetate, $\Delta^{3:5}$-cholestadien-7-one, and 12-ketocholanic acid did not react in alcohol or glacial acetic acid at 100°.

Experiments on a larger scale with cholestanone, coprostanone, cholestenone, and 3 : 12-diketocholanic acid gave products which formed insoluble enolic potassium salts and gave a purple colour with alcoholic ferric chloride.

*Cholestane*-2 : 3-*dione, Form* (*A*).—A solution of cholestanone (10 g.) in boiling alcohol (200 c.c.) was added to a hot solution of selenium dioxide (80 g.) in water (45 c.c.) and alcohol (200 c.c.). On refluxing, the mixture immediately turned yellow and a red precipitate of selenium was formed, which was removed after 15 minutes' boiling and thoroughly washed with hot alcohol (100 c.c.). The filtrate deposited a flocculent brown precipitate (1·6—1·8 g.) on cooling, which was discarded. The resulting clear yellow solution was diluted with ether (400 c.c.) and poured into half-saturated salt solution (700 c.c.). After being washed with water and saturated sodium bicarbonate solution (200 c.c.), the ethereal layer was vigorously shaken with 20% aqueous potassium hydroxide (200 c.c.) in a separating funnel, which was subsequently kept immersed in ice-water until the pale yellow precipitate of the enolic potassium salt had collected at the interface. The aqueous layer was run off, and the ethereal layer decanted from the potassium salt, which was twice washed by decantation with ether. A second extraction with 20% aqueous potassinm hydroxide (100 c.c.) of the combined ethereal layer and washings gave a further small quantity of the potassium salt. When a suspension of this salt in ether (200 c.c.) was shaken with an excess of dilute hydrochloric acid, an ethereal solution of the diosphenol was obtained, which was washed with water and dried over anhydrous sodium sulphate. On removal of the solvent in a vacuum at room temperature, the crude diosphenol was obtained as a pale yellow, crystalline solid (5·2 g.).

The product from three such preparations (15·4 g.) was dissolved in cold petrol (450 c.c.) and freed from insoluble flocculent material. On concentration to 200 c.c. at room temperature in a vacuum and after standing at 0°, the petrol solution yielded pale yellow, prismatic needles, m. p. 144—145° (8·5 g.). A further crop (2·0 g.) of the same m. p. was obtained on concentration of the mother-liquor. The product was recrystallised from glacial acetic acid, from which *cholestane*-2 : 3-*dione* (*A*) separated in prismatic needles, m. p. 144—145°, $[\alpha]_{5461}^{20°}$ + 91·5°, $[\alpha]_D^{20°}$ + 79·1° (*c*, 0·954) *; $\alpha_{5461}/\alpha_D = 1·16$ (Found †: C, 80·8; H, 10·9. $C_{27}H_{44}O_2$ requires C, 80·9; H, 11·1%). The absorption spectrum of an alcoholic solution (0·005%) is shown in the figure: maximum 2720 A., log $\varepsilon_m$ = 3·70. According to the observation made by Dr. R. K. Callow, to whom we are indebted for the spectroscopic measurements, the maxima of both forms of the diosphenol show in alkaline solution (N/200-sodium hydroxide in 95% alcohol) an equal shift in wave-length to 3200 A., log $\varepsilon_m$ = 3·57 (figure).

Form (A) of the diosphenol is readily soluble in dioxan, pyridine, and ethyl acetate, sparingly soluble in cold methyl alcohol, ethyl alcohol, or glacial acetic acid, and may be recrystallised from petrol or mixtures of pyridine, dioxan, or ethyl acetate with methyl alcohol. The Liebermann–Burchard colour reaction is given in the typical way. In the Salkowski reaction the chloroform layer remains colourless and the lower layer turns from yellow to cherry-red. A solution of form (A) in concentrated sulphuric acid is at first lemon-yellow and changes on standing to a deep cherry-red [cf. behaviour of form (B)].

After removal of the diosphenol, the residue (4 g.) of the ethereal mother-liquor was repeatedly crystallised from alcohol and yielded colourless needles, m. p. 128—129°, of cholestanone, which was characterised as the *o*-tolylsemicarbazone. This derivative is obtained in quantitative yield by dissolving the ketone (0·2 g.) and *o*-tolylsemicarbazide (0·2 g.) in alcohol (10 c.c.) containing a drop of acetic acid. After crystallisation from benzene–alcohol the colourless needles of *cholestanone*-o-*tolylsemicarbazone*, m. p. 228—229° (decomp.), showed no depression of m. p. in admixture with a specimen prepared from authentic cholestanone (Found: N, 8·0. $C_{35}H_{55}ON_3$ requires N, 7·8%).

* The optical rotations were measured in a 4 dm. tube in chloroform solutions.

† Micro-analyses by Dr. G. Weiler, Oxford.

The *monoacetate* of *form* (*A*), prepared by refluxing the diosphenol (2·7 g.) with acetic anhydride (15 c.c.) for 40 minutes, crystallised in glistening plates on cooling, and was recrystallised from 85% alcohol; m. p. 137—138°, $[\alpha]_{5461}^{18^\circ}$ + 109·8°, $[\alpha]_D^{18^\circ}$ + 91·8° (*c*, 1·138), $\alpha_{5461}/\alpha_D$ = 1·19 (Found : C, 78·7; H, 10·5. $C_{29}H_{46}O_3$ requires C, 78·7; H, 10·5%). The acetate did not react with ferric chloride, but gave, in contrast to the diosphenol, a purple colour with *m*-dinitrobenzene and alcoholic potassium hydroxide (Zimmermann, *Z. physiol. Chem.*, 1935, **233**, 257). U.V. absorption in alcohol : Maximum, 2380 A., log $\varepsilon_m$ = 3·87.

Hydrolysis was effected rapidly when sodium ethoxide (1·2 mols.) in alcohol (10 c.c.) was added to a solution of the acetate (0·5 g.) in ether (4 c.c.). The solution immediately turned yellow and after 5 minutes 50% alcohol (1·4 c.c.) was added drop by drop until crystallisation of the white sodium salt began. After cooling in the ice-box the sodium salt was collected and dissolved in warm glacial acetic acid (3·5 c.c.), from which well-formed prismatic needles of the diosphenol, form (A), m. p. 144—145°, separated on cooling.

The *monobenzoate* was obtained by dissolving the diosphenol (0·5 g.) in pyridine (12 c.c.) and adding benzoyl chloride (1 c.c.). After standing overnight, the product was isolated in the usual way and crystallised from chloroform–methyl alcohol or ethyl acetate. The benzoate was dimorphous, crystallising from ethyl acetate in prismatic needles, which on standing were gradually converted into transparent rhombic crystals; the two forms were readily interconvertible and showed identical clearing and melting points. In polarised light, in Kofler's micro-apparatus, the crystals were seen to melt to an anisotropic liquid at 162—163°, which changed to the isotropic melt at 193—194°, showing a play of colours on cooling (Found : C, 80·4; H, 9·6. $C_{34}H_{48}O_3$ requires C, 80·9; H, 9·6%).

*Bromine titration* (by the pyridine sulphate–dibromide method). After 15 minutes at room temperature, 0·0989 g. of the diosphenol absorbed 17·5 mg. of bromine (0·89 atom of Br).

*Quinoxaline derivative.* The diosphenol (50 mg.) was refluxed in alcoholic solution (2 c.c.) with *o*-phenylenediamine (50 mg.) for an hour. The solution on cooling deposited clusters of colourless plates (44 mg.), which were collected and washed with acetone. After recrystallisation from chloroform–acetone, the *quinoxaline* was obtained as clusters of colourless blades, m. p. 179—180° (Found : N, 6·2. $C_{33}H_{48}N_2$ requires N, 5·9%).

*Oxidation to the acid* $C_{27}H_{46}O_4$ (III). Hydrogen peroxide (100-vol., 3 c.c.) and 10% aqueous potassium hydroxide (6 c.c.) were added in three equal portions, at intervals of 15 minutes, to a solution of the diosphenol (0·5 g.) in alcohol (50 c.c.), which was kept gently boiling on a steam-bath. After the cooled solution had been diluted with water and extracted with ether, the acid was liberated with dilute sulphuric acid and taken up in ether. The white crystalline residue obtained on evaporation was recrystallised from ethyl acetate, from which the acid $C_{27}H_{46}O_4$ (0·5 g.) separated in transparent hemihedral crystals, m. p. 194—195°, showing no depression in admixture with an authentic specimen prepared from cholestanone (0·0998 g. required 4·4 c.c. of N/10-sodium hydroxide for neutralisation. Calc. for $C_{27}H_{46}O_4$, 4·5 c.c.).

*Cholestane-2 : 3-dione, Form* (*B*).—A solution of form (A) of the diosphenol (0·5 g.) in glacial acetic acid (2·5 c.c.) containing concentrated hydrochloric acid (0·05 c.c.) was kept on a steam-bath for a few minutes. A mixture of the two forms, m. p. 130—132°, clearing at 150°, was deposited, on cooling, in colourless prismatic needles (0·4 g.). Separation was effected by recrystallisation from ethyl acetate, from which the less soluble *form* (*B*) crystallised in clusters of needles, m. p. 168—169°, $[\alpha]_{5461}^{22^\circ}$ + 67·3°, $[\alpha]_D^{22^\circ}$ + 57·2° (*c*, 1·010); $\alpha_{5461}/\alpha_D$ = 1·18 (Found : C, 81·0; H, 11·1. $C_{27}H_{44}O_2$ requires C, 80·9; H, 11·1%). The absorption spectrum of an alcoholic solution (0·005%) has a maximum at 2700 A., log $\varepsilon_m$ = 3·93. In alkaline solution (N/200-sodium hydroxide in 95% alcohol) the same shift to a longer wave-length takes place as in form (A) (see figure).

Form (B) of the diosphenol is much less soluble than form (A) in the same solvents and dissolves in concentrated sulphuric acid with a permanent lemon-yellow colour. The Liebermann–Burchard reaction is negative and in the Salkowski reaction the lower layer turns yellow, whilst the chloroform layer remains colourless.

The *monoacetate* of *form* (*B*) was prepared by the usual technique and crystallised in colourless needles, m. p. 140—144° (Found : C, 78·6; H, 10·2. $C_{29}H_{46}O_3$ requires C, 78·7; H, 10·5%). A mixture with the acetate of form (A), m. p. 137—138°, melted at 110—114°. U.V. absorption in alcohol : Maximum, 2370 A., log $\varepsilon_m$ = 3·95.

The ferric chloride reaction was negative; with tetranitromethane a yellow colour was produced in chloroform solution.

The quinoxaline derivative of form (B), m. p. 179—180°, was produced in the same yield and under the same conditions as that of (A), with which it is identical (mixed m. p.).

The oxidation to the acid $C_{27}H_{46}O_4$ with alkaline hydrogen peroxide was effected as described above. The dicarboxylic acid was obtained in quantitative yield, m. p. and mixed m. p. 194—195°.

*Conversion of Form (B) into Form (A).*—A solution of form (B) (0·2 g.), m. p. 168—169°, in ether (10 c.c.) was shaken with 20% aqueous potassium hydroxide (5 c.c.) at 0°. The colourless potassium salt collected at the interface and was washed twice with ether by decantation, the aqueous layer having been removed previously. The suspension of the salt in ether was shaken with an excess of dilute hydrochloric acid, and the solvent removed from the washed and dried ethereal layer. The crystalline solid, m. p. 140—142°, was recrystallised from petrol (5 c.c.) and obtained in colourless needles, m. p. 143—144°, identical with form (A) of the diosphenol (mixed m. p.). On admixture with form (B), m. p. 168—169°, however, the melting point was depressed to 133—135°, clearing at 155°.

*Hydroxymethylenecholestan-3-one.*—To a suspension of powdered sodium (0·46 g.) in ether (120 c.c.) and cholestanone (7·7 g.), amyl formate (3·2 c.c.) was slowly added. A yellow solution resulted, the sodium gradually dissolving. After 12 hours, ice-water (100 c.c.) was added, and the alkaline solution was separated and extracted with ether to remove unchanged cholestanone (4 g.). The yellow aqueous layer was freed from ether by aeration and acidified with 30% acetic acid. A white granular precipitate formed immediately, which was removed and thoroughly washed with water. On crystallisation of the dried product from chloroform–methyl alcohol, *hydroxymethylenecholestanone* was obtained as a colourless microcrystalline powder, m. p. 182—184°, clearing at 195°, which gave an intense purple colour with alcoholic ferric chloride (Found: C, 81·0; H, 11·1. $C_{28}H_{46}O_2$ requires C, 81·1; H, 11·2%). Hydroxymethylenecholestanone is sparingly soluble in alcohol, ethyl acetate, and glacial acetic acid, moderately soluble in dioxan, heptane, and benzene, and easily soluble in chloroform. Conditions for its oxidation to the diosphenol are being investigated.

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## 72. *Chemical Constitution and the Dissociation Constants of Monocarboxylic Acids. Part IX.* Monosubstituted β-Phenylpropionic and Cinnamic Acids.*

By J. Frederick J. Dippy and James E. Page.

The thermodynamic dissociation constants of 23 substituted β-phenylpropionic and cinnamic acids in aqueous solution have been determined conductometrically, and these data are discussed in relation to the strengths of the corresponding benzoic and phenylacetic acids, from the point of view of the electronic theory of valency.

The linear relationship shown to exist between dissociation constants and dipole moments of substituted benzenes (Dippy, *Nature*, 1937, **139**, 591) has been satisfactorily re-examined in the light of new values of dipole moments. The substituted phenylpropionic acids also appear to conform, but in the case of the cinnamic acids there is definitely no agreement.

Earlier papers in this series (J., 1934, 161, 1888; 1935, 343; 1936, 644; 1937, 1008) have recorded thermodynamic constants for a representative number of monosubstituted benzoic and phenylacetic acids, and the study has now been extended to the β-phenylpropionic and cinnamic series. It was expected that the acids of the phenylpropionic class would provide confirmation of the influences observed in the phenylacetic series, and this anticipation has been realised although the relative differences are naturally smaller. The *m*- and *p*-substituted cinnamic acids (all of which possess the *trans*-form) are, in the main, comparable to the corresponding benzoic acids. It has also been shown that "ortho-effects" are restricted to the benzoic series.

Table I, showing the strengths ($10^5K_{therm.}$) of methyl-, methoxy-, chloro-, and nitro-acids in the four series, provides a fairly complete set of data. For reference purposes the

* Two previous papers, *viz.*, J., 1937, 1426, 1774, which appeared under other titles are regarded as Parts VII and VIII of this series.

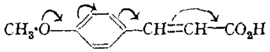
ratios $K/K_{unsub.}$ are included ($K_{unsub.}$, the thermodynamic constant of the parent acid in each series, is shown in parentheses in each heading); these simplify the examination of the relative effects of substituents from system to system.

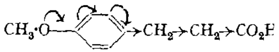
TABLE I.

| | Me. | | MeO. | | Cl. | | $NO_2$. | |
|---|---|---|---|---|---|---|---|---|
| | $10^5 K$. | $K/K_{unsub.}$ | $10^5 K$. | $K/K_{unsub.}$ | $10^5 K$. | $K/K_{unsub.}$ | $10^5 K$. | $K/K_{unsub.}$ |
| *Benzoic acids* (H, 6·27 × $10^{-5}$). | | | | | | | | |
| *o*- ............ | $12·3_5$ | 1·97 | 8·06 | 1·29 | 114 | 18·2 | 671 | 107 |
| *m*- ............ | 5·35 | 0·87 | 8·17 | 1·30 | 14·8 | 2·36 | 32·1 | 5·19 |
| *p*- ............ | 4·24 | 0·68 | 3·38 | 0·54 | $10·5_3$ | 1·68 | 37·6 | 6·00 |
| *Phenylacetic acids* (H, 4·88 × $10^{-6}$). | | | | | | | | |
| *o*- ............ | — | — | — | — | 8·60 | 1·76 | 9·90 | 2·03 |
| *m*- ............ | — | — | — | — | 7·24 | 1·48 | 10·8 | 2·21 |
| *p*- ............ | 4·27 | 0·87 | 4·36 | 0·89 | 6·45 | 1·32 | 14·1 | 2·89 |
| *β-Phenylpropionic acids* (H, 2·19 × $10^{-5}$). | | | | | | | | |
| *o*- ............ | 2·17 | 1·00 | 1·57 | 0·72 | 2·65 | 1·21 | $3·13_5$ | 1·44 |
| *m*- ............ | $2·10_5$ | 0·96 | 2·22 | 1·01 | 2·60 | 1·19 | — | — |
| *p*- ............ | 2·07 | 0·94 | $2·04_5$ | 0·94 | 2·47 | 1·13 | $3·36_5$ | 1·54 |
| *Cinnamic acids* (H, 3·65 × $10^{-5}$). | | | | | | | | |
| *o*- ............ | $3·16_5$ | 0·87 | 3·45 | 0·94 | 5·83 | 1·60 | 7·07 | 1·94 |
| *m*- ............ | $3·61_5$ | 1·00 | 4·21 | 1·15 | $5·08_5$ | 1·39 | 7·58 | 2·08 |
| *p*- ............ | 2·73 | 0·75 | 2·89 | 0·79 | 3·86 | 1·06 | 8·99 | 2·46 |

Except in the case of o-toluic acid, where an "ortho-effect" exists, introduction of methyl into *o*-, *m*-, or *p*-positions in all four acids leads to a decrease in strength. A marked fall in effect is observed in passing from *p*-toluic to the corresponding phenylacetic acid, and very little further decrease in the β-phenylpropionic acid, but *p*-methyl substitution in cinnamic acid causes a diminution as marked as in the benzoic acid; this must be attributed to the existence of the conjugate system, which permits transfer of the electromeric displacements set up by methyl. With regard to *o*-substitution, *o*-methyl-phenylpropionic and -cinnamic acids, in contrast to *o*-toluic acid, tend to be weaker than the parent acids.

The strength of *m*-methoxy-β-phenylpropionic acid is identical with that of the parent acid; the $-I$ effect of methoxyl is too weak to influence carboxyl at that distance. In the less rigid cinnamic acid system, however, *m*-methoxyl enhances the strength appreciably. The order of strengths throughout the four series is *m*-OMe > H > *o*- and *p*-OMe (except with *o*-methoxybenzoic acid, which is stronger than the parent acid), and this is in harmony with the known influence of methoxyl which combines $-I$ and $+T$ effects. The latter is pronounced, *e.g.*, in (I), and can lead to an inductively transmitted effect in a saturated side chain, *e.g.*, in (II) (cf. J., 1935, 346). It is strange, indeed, that *o*-methoxyl causes a much greater relative fall in strength in β-phenylpropionic than in cinnamic acid.

(I.) 

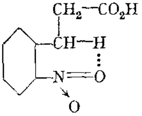
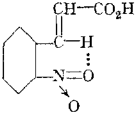
(II.) 

The strengths of *o*- and *m*-hydroxycinnamic acids have also been determined ($10^5K_{therm.}$ = 2·44 and $4·00_5$ respectively), and from these data it may be concluded that there is greate electron recession from o-hydroxyl than from *o*-methoxyl, and smaller electron accession t *m*-hydroxyl than to *m*-methoxyl. Comparison of the strengths of *m*- and *p*-hydroxy- an -methoxy-benzoic acids (in water or aqueous alcohol) leads to a similar conclusion (fo obvious reasons *p*-methoxyl is considered here in place of *o*-methoxyl). Branch an Yabroff (*J. Amer. Chem. Soc.*, 1934, **56**, 2568) published the following values of $10^5K_{therm}$ for 25% ethyl-alcoholic solution at 25°: H, 2·29; *m*-OH, 2·43; *p*-OH, 0·750; *m*-OCH 2·87; *p*-$OCH_3$, 1·16. On fundamental grounds, methyl, when substituted in hydroxy should produce results quite contrary to these. This observation is not without paralle Groves and Sugden (J., 1937, 1992) have shown that hydroxyl, when attached to the benzer nucleus, possesses a greater mesomeric moment than methoxyl, and again, it is well know

that phenol undergoes substitution far more readily than anisole. It is not possible to explain the anomalous order of strengths, *o*-OMe > *o*-OH and *m*-OMe > *m*-OH in these aromatic acids on the basis of ionisation of the hydroxyl group. This ionisation would lead to relatively *high* constants in the hydroxy-acids, whereas low constants are actually the case. Moreover, the second dissociation constant of salicylic acid has been shown by Senter and Bulle (J., 1912, **101**, 2532) to be of the order of $1 \times 10^{-13}$ (cf. Branch and Yabroff, *loc. cit.*), and it is likely that other phenolic acids are comparable in this respect.

In all four series the order of strengths of chloro-acids is *o*- > *m*- > *p*- > H, and as far as we have determined, the other halogeno-acids preserve a similar order. The much discussed " mesomeric " effect of halogen (compare in this connection the work of Groves and Sugden, *loc. cit.*) contributes to the order *m*- > *p*-, but there seems to be no particular reason why the *o*-acid should consistently be the strongest of the three. In accordance with anticipation, the ratio $K/K_{\text{unsub.}}$ is greater in benzoic and cinnamic acids than in phenylacetic and phenylpropionic acids, irrespective of whether the chlorine occupies the *o*-, *m*-, or *p*-position.

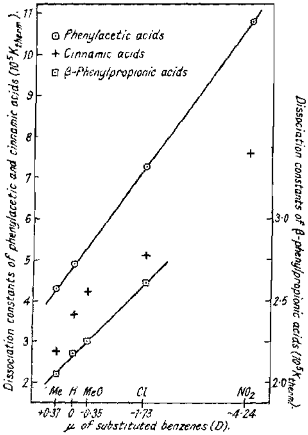
The order of strengths of the nitro-acids (the abnormal *o*-nitrobenzoic acid being omitted) is *p*- > *m*- > *o*- > H, but on the basis of the operation of the $-I$ and the $-T$ effect of nitroxyl, it is reasonable to suppose that the *o*-nitro-acids should be comparable with the *p*-nitro-isomerides in being stronger than the *m*-acids (the phenylacetic and phenylpropionic acids are included in this because the $-T$ effect of nitroxyl is believed to be transmitted inductively through a saturated side chain; see reference to methoxyl above). Dippy and Lewis (J., 1937, 1426), studying the nitrophenylacetic acids, first showed the *o*-isomeride to be the weakest, and to account for this feature they suggested that the molecule was chelated along the lines already suggested for *o*-nitrotoluene by Sidgwick and Callow (J., 1924, **125**, 538). This chelation may also occur in *o*-nitrophenylpropionic (III) and *o*-nitrocinnamic acids (IV), and it is significant that the constants of these acids are now found to be anomalous.

(III.)  (IV.) 

The strength of 3-nitro-*o*-toluic acid has been determined by us ($10^2K_{\text{therm.}} = 1{\cdot}335$), and this demonstrates that the introduction of a second *o*-substituent into an acid further enhances the strength abnormally. The increase brought about in *o*-toluic acid (which itself exhibits an " ortho-effect ") by substituting nitroxyl in the *o*-position to the carboxyl group is even greater than that observed in going from benzoic to *o*-nitrobenzoic acid. The dissociation constants of two other 2 : 6-disubstituted benzoic acids may be found in the literature, *viz.*, the dihydroxy- ($10^2K_{\text{class.}} = 5{\cdot}0$; Ostwald, *Z. physikal. Chem.*, 1889, **3**, 249) and the dinitro- ($10^2K_{\text{class.}} = 8{\cdot}15$; Sirks, *Rec. trav. chim.*, 1908, **27**, 221) acid, and these also indicate the trend observed above. It should be noted that the thermodynamic dissociation constant for 3-nitro-*o*-toluic acid is substantially greater than that of the classical constant ($1{\cdot}135 \times 10^{-2}$), and this may be expected in an acid of this order of strength (compare remarks on *o*-nitrobenzoic acid, J., 1937, 1426). Further, the values of $K_{\text{therm.}}$ for the other diortho-substituted acids cited here would be greatly in excess of the recorded values, which are in terms of $K_{\text{class.}}$; this favours still more the foregoing observation.

*Quantitative Correlation.*—It has already been pointed out by one of us (*Nature*, 1937, **139**, 591) that a linear relationship exists between the dissociation constants ($K_{\text{therm.}}$) of *m*-nitro-, *m*-chloro-, *m*-methoxy-, *p*-methyl, and unsubstituted benzoic and phenylacetic acids and the dipole moments of substituted benzenes (the values were all comparable but referred to benzene solution; see J., 1937, 1008, for figure). This relationship is now re-examined in the light of recent measurements on the vapours of these substituted benzenes and the results are included in the figure. The benzoic and phenylacetic acids give excellent conformity; the relationship has also been tested with β-phenylpropionic acids, as far as

data permit, and found to hold good. In the case of the phenylacetic and β-phenylpropionic acids it can be shown that if the dipole moments of substituted toluenes (data for benzene solution) are taken, a straight line is also obtained. From this it follows that, where the side chain of the acid is composed of methylene links, the dipole moments of substituted benzenes constitute a satisfactory basis for correlation. It is seen from the figure, however, that the points representing the cinnamic acids are irregular, meaning that the permanent polar influences operating in the acids here are not reflected truly in these dipole moments; this is not surprising, since the existence of a double bond in the side chain must considerably affect the polarity of the molecule. The effect of introducing two methylene carbon atoms into a chain is very different from that of introducing vinyl, which is recognised to possess a strong intrinsic attraction for electrons (this is illustrated in the strengths of unsaturated acids; Dippy and Lewis, J., 1937, 1008). Unfortunately, dipole-moment data for the appropriate styrenes do not exist, and so further examination of the cinnamic acids cannot be made.




*The values of μ are due to Groves and Sugden* (J., 1935, 971; 1937, 1992) *except that for toluene* (*McAlpine and Smyth*, J. Amer. Chem. Soc., 1933, **55**, 453). *In the case of anisole the effective moment is taken to be given by μ × cos 105°* (*cf.* Chem. and Ind., 1935, **54**, 736).

*The Mobilities of Anions.*—A comprehensive survey of the mobilities of the anions of common aromatic monobasic acids is now possible. It has been made abundantly clear that isomeric ions differ in mobility, although there does not appear to be any rule as to the effect on the speed of migration brought about by moving the position of the substituent examination of ion mobilities in the four series fails to reveal any consistent order Constitutive influences must be partly responsible for the movement of anions, since it i obvious that considerations of bulk and weigh do not always provide an explanation. It i seen that the mobilities of methyl- an methoxyl-substituted ions are, on the whol smaller than might be expected, when con pared with the mobilities of halogen- an nitro-substituted anions. Nevertheless, ic size plays quite an important part, and it has been shown that the speed does not reach limit when the anion contains 12 atoms (the original postulate of Ostwald). Actually, very appreciable fall in mobility has been observed when bulky substituents such phenyl and phenoxyl are introduced into the benzoate ion (a decrease of 33·4 to 23·5 a 23·3, respectively; Dippy and Lewis, *loc. cit.*).

## EXPERIMENTAL.

Conductivity measurements were made on aqueous solutions of 24 acids and their salts at by the procedure described earlier (Parts I—III). The cells were calibrated frequently, and constants calculated on the customary Parker–Parker basis. The conductivity water emplo throughout had a specific conductivity of 0·9—1·0 gemmho.

The stock solutions of almost all the phenylpropionic acids were made up to 500 ml., wher those of most of the cinnamic acids were made up to 1 l. The only acids soluble enough permit the preparation of 250 ml. of solution were 3-nitro-*o*-toluic and *o*-chloro-β-phe propionic acids; it is indeed surprising that the disubstituted benzoic acid has such a relati high solubility.

Values of $\Lambda_0$ (salt) were computed from the sodium salt measurements by the metho Dippy and Williams (see Parts I and II).

TABLE II.

*o-Methyl-β-phenylpropionic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·1347 | 1·002 | 52·01 | 2·20$_5$ | 2·16$_5$ |
| | 0·5835 | 66·21 | 2·17$_5$ | 2·14 |
| | 0·5595 | 67·81 | 2·19$_5$ | 2·15$_5$ |
| 0·07288 | 0·4094 | 77·38 | 2·16 | 2·13 |
| | 0·2814 | 91·49 | 2·18 | 2·15$_5$ |

12 Detmtns.; limits of $10^5 K_{therm.}$ 2·13—2·21; $\Lambda_0$ (acid) = 377·8.

*p-Methyl-β-phenylpropionic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·1365 | 0·7537 | 58·01 | 2·09$_5$ | 2·06 |
| | 0·5584 | 66·46 | 2·09$_5$ | 2·06 |
| | 0·4139 | 75·58 | 2·06$_5$ | 2·04 |
| 0·07394 | 0·2650 | 92·15 | 2·08 | 2·05$_5$ |
| | 0·1969 | 104·5 | 2·08 | 2·05$_5$ |

15 Detmtns.; limits of $10^5 K_{therm.}$ 2·03—2·11; $\Lambda_0$ (acid) = 378·1.

*m-Methoxy-β-phenylpropionic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·1349 | 0·4977 | 72·63 | (2·29) | 2·25$_5$ |
| | 0·2828 | 92·51 | 2·25$_5$ | 2·23 |
| | 0·1902 | 109·3 | 2·25 | 2·23 |
| 0·07288 | 0·1716 | 113·4 | 2·22 | 2·20 |
| | 0·1051 | 137·7 | 2·21 | 2·19 |

11 Detmtns.; limits of $10^5 K_{therm.}$ 2·19—2·25$_5$; $\Lambda_0$ (acid) = 377·0.

*o-Chloro-β-phenylpropionic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·1347 | 0·6699 | 68·69 | 2·70 | 2·65$_5$ |
| | 0·3229 | 95·04 | 2·72 | 2·69 |
| | 0·2803 | 100·1 | 2·67$_5$ | 2·64 |
| 0·07288 | 0·2202 | 110·4 | 2·65$_5$ | 2·62 |
| | 0·1795 | 120·4 | 2·67$_5$ | 2·64$_5$ |

10 Detmtns.; limits of $10^5 K_{therm.}$ 2·62—2·69; $\Lambda_0$ (acid) = 378·1.

*p-Chloro-β-phenylpropionic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·1347 | 0·5139 | 74·50 | 2·49$_5$ | 2·46 |
| | 0·2509 | 101·7 | 2·50 | 2·47 |
| | 0·2439 | 102·3 | 2·46 | 2·43$_5$ |
| 0·07288 | 0·1758 | 118·4 | 2·52 | 2·49$_5$ |
| | 0·08921 | 153·9 | 2·50$_5$ | 2·48$_5$ |

11 Detmtns.; limits of $10^5 K_{therm.}$ 2·43$_5$—2·49$_5$. $\Lambda_0$ (acid) = 377·4.

*p-Nitro-β-phenylpropionic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·07214 | 0·3421 | 102·6 | 3·44 | 3·39 |
| | 0·2667 | 114·2 | 3·46$_5$ | 3·42 |
| | 0·2122 | 123·8 | 3·36$_5$ | 3·33 |
| 0·05284 | 0·1724 | 135·0 | 3·40 | 3·36$_5$ |
| | 0·1393 | 146·1 | 3·36$_5$ | 3·33 |

12 Detmtns.; limits of $10^5 K_{therm.}$ 3·33—3·42$_5$. $\Lambda_0$ (acid) = 379·0.

*m-Methylcinnamic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·1343 | 0·6459 | 80·17 | 3·66$_5$ | 3·61 |
| | 0·3210 | 108·6 | 3·69$_5$ | 3·65 |
| | 0·2878 | 113·9 | 3·71$_5$ | 3·66$_5$ |
| 0·07295 | 0·2044 | 130·3 | 3·68 | 3·63 |
| | 0·1499 | 146·6 | 3·65$_5$ | 3·60 |
| | 0·1353 | 152·3 | 3·65 | 3·60 |

11 Detmtns.; limits of $10^5 K_{therm.}$ 3·56—3·67; $\Lambda_0$ (acid) = 379·1.

*o-Hydroxycinnamic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·1347 | 0·7233 | 63·90 | 2·49 | 2·45 |
| | 0·5229 | 73·41 | 2·45 | 2·41$_5$ |
| | 0·4179 | 81·00 | 2·44$_5$ | 2·41$_5$ |
| 0·07288 | 0·2873 | 95·94 | 2·48$_5$ | 2·45$_5$ |
| | 0·1682 | 119·9 | 2·48 | 2·45$_5$ |

11 Detmtns.; limits of $10^5 K_{therm.}$ 2·41$_5$—2·45$_5$; $\Lambda_0$ (acid) = 377·8.

*m-Methyl-β-phenylpropionic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·1338 | 0·5024 | 70·86 | 2·18 | 2·14$_5$ |
| | 0·3925 | 78·48 | 2·14 | 2·11$_5$ |
| | 0·2492 | 95·79 | 2·15 | 2·12$_5$ |
| 0·07214 | 0·1515 | 116·7 | 2·09 | 2·07 |
| | 0·1110 | 133·1 | 2·13 | 2·11$_5$ |

10 Detmtns.; limits of $10^5 K_{therm.}$ 2·06$_5$—2·14$_5$; $\Lambda_0$ (acid) = 377·6.

*o-Methoxy-β-phenylpropionic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·1349 | 0·5134 | 60·91 | 1·59$_5$ | 1·57$_5$ |
| | 0·4663 | 63·74 | 1·60$_5$ | 1·58$_5$ |
| | 0·3177 | 75·67 | 1·60$_5$ | 1·58 |
| 0·07254 | 0·2140 | 89·54 | 1·58 | 1·56$_5$ |
| | 0·1768 | 97·16 | 1·58 | 1·56$_5$ |

12 Detmtns.; limits of $10^5 K_{therm.}$ 1·54$_5$—1·58$_5$; $\Lambda_0$ (acid) = 377·2.

*p-Methoxy-β-phenylpropionic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·1349 | 0·5822 | 64·91 | 2·08$_5$ | 2·05$_5$ |
| | 0·4818 | 70·84 | 2·09$_5$ | 2·06$_5$ |
| | 0·4490 | 72·88 | 2·08 | 2·05$_5$ |
| | 0·3697 | 79·68 | 2·09$_5$ | 2·07 |
| 0·07254 | 0·2773 | 89·86 | 2·07 | 2·04$_5$ |
| | 0·2070 | 101·6 | 2·06 | 2·04 |

11 Detmtns.; limits of $10^5 K_{therm.}$ 2·02—2·07; $\Lambda_0$ (acid) = 377·0.

*m-Chloro-β-phenylpropionic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·1338 | 0·3902 | 86·72 | 2·67 | 2·63$_5$ |
| | 0·3087 | 95·50 | 2·64 | 2·61 |
| | 0·2292 | 107·6 | 2·60 | 2·57 |
| 0·07214 | 0·2107 | 111·0 | 2·57$_5$ | 2·55 |
| | 0·1548 | 126·4 | 2·60$_5$ | 2·58 |

11 Detmtns.; limits of $10^5 K_{therm.}$ 2·55—2·63$_5$; $\Lambda_0$ (acid) = 377·8.

*o-Nitro-β-phenylpropionic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·1347 | 0·3897 | 93·89 | 3·19 | 3·14$_5$ |
| | 0·2888 | 106·5 | 3·18$_5$ | 3·14$_5$ |
| | 0·2335 | 116·1 | 3·17 | 3·13$_5$ |
| 0·07288 | 0·1613 | 134·8 | 3·17$_5$ | 3·14 |
| | 0·1413 | 142·0 | 3·18$_5$ | 3·15 |

10 Detmtns.; limits of $10^5 K_{therm.}$ 3·12—3·15; $\Lambda_0$ (acid) = 378·4.

*o-Methylcinnamic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·07288 | 0·09350 | 166·2 | 3·17$_5$ | 3·15 |
| | 0·07391 | 180·1 | 3·15$_5$ | 3·13 |
| 0·05347 | 0·06112 | 192·1 | 3·16 | 3·14 |
| | 0·05319 | 202·1 | 3·21$_5$ | 3·19$_5$ |

8 Detmtns.; limits of $10^5 K_{therm.}$ 3·13—3·23; $\Lambda_0$ (acid) = 380·0.

*p-Methylcinnamic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·07246 | 0·1234 | 142·9 | 2·81$_5$ | 2·79$_5$ |
| | 0·1060 | 151·5 | 2·82 | 2·80 |
| | 0·1019 | 154·4 | 2·85 | 2·83 |
| 0·05319 | 0·07787 | 168·1 | 2·74$_5$ | 2·73 |
| | 0·06871 | 171·7 | (2·57$_5$) | (2·56) |

10 Detmtns.; limits of $10^5 K_{therm.}$ 2·64—2·83; $\Lambda_0$ (acid) = 379·1.

*m-Hydroxycinnamic acid.*

| Cell const. | $10^3 C$. | Λ. | $10^5 K_{class.}$ | $10^5 K_{therm.}$ |
|---|---|---|---|---|
| 0·1347 | 0·5610 | 88·9 | 4·06 | 3·99$_5$ |
| | 0·3290 | 111·5 | 4·06 | 4·00 |
| | 0·2994 | 115·2 | (4·00) | 3·95 |
| 0·07288 | 0·2152 | 133·5 | 4·14$_5$ | 4·09$_5$ |
| | 0·1769 | 142·8 | 4·05$_5$ | 4·01 |

10 Detmtns.; limits of $10^5 K_{therm.}$ 3·95—4·09$_5$; $\Lambda_0$ (acid) = 378·0.

TABLE II (*contd.*).

| Cell const. | $10^3$ *C*. | Λ. | $10^5$ $K_{class.}$ | $10^5$ $K_{therm.}$ |
|---|---|---|---|---|
| | | *o-Methoxycinnamic acid.* | | |
| 0·07246 | 0·1331 | 150·9 | 3·53$_5$ | 3·49$_5$ |
| | 0·1326 | 150·7 | 3·51 | 3·47 |
| | 0·1278 | 149·4 | 3·30$_5$ | (3·26$_5$) |
| | 0·1140 | 158·4 | 3·45$_5$ | 3·42 |
| 0·05319 | 0·09452 | 169·3 | 3·44 | 3·41 |
| | 0·07741 | 182·0 | 3·46$_5$ | 3·43 |

10 Detmtns.; limits of $10^5$ $K_{therm.}$ 3·38$_5$—3·54; $\Lambda_0$ (acid) = 377·8.

| Cell const. | $10^3$ *C*. | Λ. | $10^5$ $K_{class.}$ | $10^5$ $K_{therm.}$ |
|---|---|---|---|---|
| | | *p-Methoxycinnamic acid.* | | |
| 0·07254 | 0·1163 | 147·2 | 2·92$_5$ | 2·90 |
| | 0·1069 | 153·9 | 3·02 | 3·00 |
| | 0·09033 | 165·8 | (3·11$_5$) | (3·09$_5$) |
| 0·05319 | 0·07467 | 171·6 | 2·85 | 2·83 |
| | 0·06236 | 186·2 | 3·01 | 2·99 |

11 Detmtns.; limits of $10^5$ $K_{therm.}$ 2·84—3·00; $\Lambda_0$ (acid) = 376·6.

| Cell const. | $10^3$ *C*. | Λ. | $10^5$ $K_{class.}$ | $10^5$ $K_{therm.}$ |
|---|---|---|---|---|
| | | *o-Nitrocinnamic acid.* | | |
| 0·1351 | 0·3181 | 143·0 | 7·34 | 7·24 |
| | 0·2629 | 153·4 | 7·30 | 7·20 |
| | 0·1759 | 175·7 | 7·11 | 7·03 |
| 0·7278 | 0·1279 | 194·5 | 6·99 | 6·93 |
| | 0·07668 | 199·7 | 7·22 | 7·17 |

10 Detmtns.; limits of $10^5$ $K_{therm.}$ 6·87—7·24; $\Lambda_0$ (acid) = 377·8.

| Cell const. | $10^3$ *C*. | Λ. | $10^5$ $K_{class.}$ | $10^5$ $K_{therm.}$ |
|---|---|---|---|---|
| | | *p-Nitrocinnamic acid.* | | |
| 0·07259 | 0·07252 | 248·9 | 9·20 | 9·15 |
| | 0·06146 | 258·9 | 9·14 | 9·09 |
| | 0·05198 | 267·9 | 8·95 | 8·90 |
| 0·05351 | 0·05129 | 269·2 | 9·02 | 8·98 |
| | 0·04141 | 280·9 | 8·89 | 8·86 |

9 Detmtns.; limits of $10^5$ $K_{therm.}$ 8·75—9·15; $\Lambda_0$ (acid) = 378·1.

| Cell const. | $10^3$ *C*. | Λ. | $10^5$ $K_{class.}$ | $10^5$ $K_{therm.}$ |
|---|---|---|---|---|
| | | *m-Methoxycinnamic acid.* | | |
| 0·1347 | 0·3483 | 110·8 | 4·25$_5$ | 4·19$_5$ |
| | 0·2400 | 128·8 | 4·25$_5$ | 4·20$_5$ |
| | 0·1952 | 140·3 | 4·30 | 4·25 |
| 0·07288 | 0·1498 | 154·1 | 4·23$_5$ | 4·19 |
| | 0·1074 | 175·8 | 4·22$_5$ | 4·18 |

12 Detmtns.; limits of $10^5$ $K_{therm.}$ 4·18—4·25$_5$; $\Lambda_0$ (acid) = 377·1.

| Cell const. | $10^3$ *C*. | Λ. | $10^5$ $K_{class.}$ | $10^5$ $K_{therm.}$ |
|---|---|---|---|---|
| | | *m-Chlorocinnamic acid.* | | |
| 0·07259 | 0·1539 | 163·2 | 5·09 | 5·05 |
| | 0·1346 | 173·3 | (5·26) | (5·21) |
| | 0·1276 | 175·9 | 5·21 | 5·16 |
| 0·05351 | 0·1050 | 186·9 | 5·12 | 5·09 |
| | 0·09942 | 190·5 | 5·14 | 5·10 |

10 Detmtns.; limits of $10^5$ $K_{therm.}$ 4·94—5·16; $\Lambda_0$ (acid) = 377·0.

| Cell const. | $10^3$ *C*. | Λ. | $10^5$ $K_{class.}$ | $10^5$ $K_{therm.}$ |
|---|---|---|---|---|
| | | *m-Nitrocinnamic acid.* | | |
| 0·07285 | 0·1264 | 203·7 | 7·80 | 7·73 |
| | 0·1170 | 208·8 | 7·78 | 7·72 |
| | 0·1162 | 208·6 | 7·74 | 7·67 |
| | 0·09768 | 217·9 | (7·49) | 7·43 |
| | 0·07914 | 233·5 | 7·72 | 7·67 |

12 Detmtns.; limits of $10^5$ $K_{therm.}$ 7·38—7·73; $\Lambda_0$ (acid) = 380·5.

| Cell const. | $10^3$ *C*. | Λ. | $10^5$ $K_{class.}$ | $10^5$ $K_{therm.}$ |
|---|---|---|---|---|
| | | *3-Nitro-o-toluic acid.* | | |
| 0·1347 | 0·7667 | 354·0 | 1110 | 1265 |
| | 0·4369 | 362·4 | 1043 | 1275 |
| | 0·3708 | 366·7 | 1285 | (1575) |
| 0·07288 | 0·2435 | 369·1 | 1115 | 1500 |
| | 0·1593 | 370·8 | (937·5) | 1340 |

15 Detmtns.; limits of $10^5$ $K_{therm.}$ 1230—1500; $\Lambda_0$ (acid) = 377·0. A higher degree of accuracy could not be achieved for this highly-conducting acid.

Table II contains details of the experimental results on acids. In each case a representative run is included, together with the mean value of $\Lambda_0$ (acid) obtained by employing the usual sodium and hydrogen mobilities; the concentration *C* refers to g.-equivs. per litre.

The values in parentheses in the above table were not taken into account in the calculation of mean constants.

*Preparation of Materials.*—All the β-phenylpropionic acids, except the nitro-derivatives were obtained by reduction of aqueous solutions of salts of the corresponding cinnamic acids In each case the cinnamic acid (1 mol.) was dissolved in sodium hydroxide solution and treatec with 2½% sodium amalgam (4 atoms) in small portions with intermittent shaking. The whol was then heated for 1 hour on a steam-bath to ensure complete reaction of the sodium amalgam the aqueous layer decanted and treated with concentrated hydrochloric acid in the cold, and th precipitated phenylpropionic acid washed and recrystallised from water. Yields of 80—90% were frequently obtained.

*o*- and *p*-Nitro-β-phenylpropionic acids had to be prepared by nitration of the parent aci with a mixture of concentrated and fuming nitric acid (Konek and Pascu, *Ber.*, **1918**, **51**, 858 The yields of pure acid were 20% and 50% respectively.

*o*- and *p*-Methyl-, *m*-hydroxy-, and *o*-, *m*-, and *p*-methoxy-cinnamic acids were prepared b the Knoevenagel synthesis, which proved to be clean and economical. The general procedu was as follows: An alcoholic solution of the substituted benzaldehyde (1 mol.) and malonic ac (1·5 mols.) was treated with 7% alcoholic ammonia solution (1 mol. of $NH_3$), and allowed stand for 24 hrs. The alcohol was evaporated, and the residue (intermediate malonic ac derivative) decomposed by heating to 100—120°. The remaining acid was extracted wi sodium carbonate solution and recovered by acidification. Precautions had to be taken wi *o*-hydroxybenzaldehyde to exclude air to the utmost, since oxidation occurred very readi Yields of 70—80% of substituted cinnamic acid were obtained throughout.

Attempts to prepare these acids by the haloform reaction met with little success. Hitherto, the Perkin synthesis has been applied almost exclusively.

*m*-Methoxycinnamic acid had to be prepared by methylation, and the method described here is superior to those in the literature. *m*-Hydroxycinnamic acid (1 mol.) was dissolved in a large excess of concentrated sodium hydroxide solution, and methyl sulphate (4 mols.) added gradually with shaking; after being warmed on the steam-bath for 2 hrs., the solution was extracted with ether and the aqueous layer acidified, whereupon the methoxy-acid was precipitated (70% yield).

We are indebted to Professor F. Böck of the Technische Hochschule, Vienna, for specimens of *m*-methyl-, *m*-chloro-, and *o*-, *m*-, and *p*-nitro-cinnamic acids, and to Professor L. P. Hammett, of Columbia University, for the 3-nitro-*o*-toluic acid.

All acids were finally purified by recrystallisation several times from conductivity water and drying in a vacuum desiccator. They were kept out of contact with light as far as possible; certain of the substituted cinnamic acids (*e.g.*, the nitro-acid) develop a reddish colour after long exposure to daylight. Details of the purity of the dry acids used in the measurements are included in Table III. The equivalents of all acids were determined by titration.

TABLE III.

| | M. p. (corr.). | M. p. (best in lit.). | |
|---|---|---|---|
| *β-Phenylpropionic acids.* | | | |
| *o*-Me | 102° | 102° | (Young, *Ber.*, 1892, **25**, 2104) |
| *m*-Me | 43 | 42—43 | (v. Miller and Rohde, *ibid.*, 1890, **23**, 1899) |
| *p*-Me | 122 | 120 | (Kröber, *ibid.*, p. 1033) |
| *o*-OMe | 92 | 92 | (Perkin, J., 1881, **39**, 415) |
| *m*-OMe | 52 | 51 | (Tiemann and Ludwig, *Ber.*, 1882, **15**, 2052) |
| *p*-OMe | 107 | 104—105 | (Borsche and Gerhardt, *ibid.*, 1914, **47**, 2914) |
| *o*-Cl | 99 | 97 | (Stoermer, *ibid.*, 1911, **44**, 659) |
| *m*-Cl | 77 | 77—78 | (Gabriel and Herzberg, *ibid.*, 1883, **16**, 2039) |
| *p*-Cl | 126 | 124 | (*Idem, ibid.*) |
| *o*-$NO_2$ | 115 | 115 | (Jaenisch, *ibid.*, 1923, **56**, 2448) |
| *p*-$NO_2$ | 168 | 163—164 | (Beilstein and Kuldberg, *Annalen*, 1872, **163**, 132) |
| *Cinnamic acids.* | | | |
| *o*-Me | 169 | 174—175 | (v. Auwers, *ibid.*, 1917, **413**, 265) |
| | | 169 | (Böck, Lock, and Schmidt, *Monatsh.*, 1934, **64**, 399) |
| *m*-Me | 119 | 118 | (*Idem, ibid.*) |
| *p*-Me | 199 | 198—199 | (Hanzlik and Bianchi, *Ber.*, 1899, **32**, 1289) |
| | | 199 | (Böck, Lock, and Schmidt, *loc. cit.*) |
| *o*-OH | 209 | 214 | (Stoermer, *Ber.*, 1911, **44**, 643) |
| | | 208 | (Fittig and Ebert, *Annalen*, 1884, **226**, 351) |
| *m*-OH | 194 | 193 | (Posner, *J. pr. Chem.*, 1910, **82**, 428) |
| *o*-OMe | 186 | 185—186 | (Reychler, *Bull. Soc. chim.*, 1908, **3**, 552) |
| *m*-OMe | 120 | 117 | (Bauer and Vogel, *J. pr. Chem.*, 1913, **88**, 340) |
| *p*-OMe | 174 | 173·8 | (Prins, *Z. physikal. Chem.*, 1909, **67**, 718) |
| *m*-Cl | 167 | 176 | (Gabriel and Herzberg, *loc. cit.*) |
| | | 165 | (Böck, Lock, and Schmidt, *loc. cit.*) |
| *o*-$NO_2$ | 242 | 242 | (*Idem, ibid.*) |
| *m*-$NO_2$ | 202 | 201 | (*Idem, ibid.*) |
| *p*-$NO_2$ | 288 | 288 | (Drewsen, *Annalen*, 1882, **212**, 151; Böck, Lock, and Schmidt, *loc. cit.*) |
| 3-Nitro-*o*-toluic acid | 154 | 153—154 | (Treffers and Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 1709) |

The strengths ($10^5 K_{class.}$) of only three of the above acids have hitherto been measured. Roth and Stoermer (*Ber.*, 1913, **46**, 267) recorded a value of 2·1 for both *o*- and *p*-methoxycinnamic acids, whereas we found classical constants of 3·47 and $2{\cdot}91_8$ respectively; the value of $\Lambda_0$ (acid) in each case, *viz.*, 369, was also very considerably lower than our figure. The dissociation constant of *o*-hydroxycinnamic acid has been given as 2·14 and 2·7 by Ostwald (*Z. physikal. Chem.*, 1889, **3**, 277) and Springer and Jones (*Amer. Chem. J.*, 1912, **48**, 441), respectively (our classical constant is 2·48).

The following points are also noteworthy: (1) the order of m. p.'s of the above isomeric acids is *p*- > *o*- > *m*- (excluding the methoxycinnamic acids), (2) the sodium salt solution prepared from *o*-hydroxycinnamic acid exhibited a pronounced yellow-green fluorescence (cf. Zwenger, *Annalen*, 1872, Suppl. **8**, 23).

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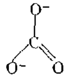
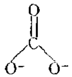
# 73. *Diamagnetic Anisotropy of Conjugated Compounds.*

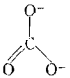
By (Mrs.) Kathleen Lonsdale.

In order to extend quantitative knowledge of crystal susceptibilities to different types of conjugated compounds, data are given for metal-free phthalocyanine, oxalic acid dihydrate, stilbene, tolan, and *trans*-azobenzene. These have been correlated with the available *X*-ray data for the molecular direction cosines in order to obtain the principal susceptibilities of the molecules. The anisotropy of the oxalate group is about twice that of the carbonate radical and about one-sixth of that of benzene. Stilbene and tolan possess, not only the expected anisotropy normal to the molecular plane, which may be explained in terms of molecular orbitals, but also a considerable anisotropy *in* that plane, which is not yet explained. It is shown that large diamagnetic anisotropy is associated with the existence of bond resonance (mesomerism), plane arrangement of atoms in the molecule and tendency to equalisation of bond distances, not only in closed rings (as predicted by theory) but also in open systems.

Recent studies, both experimental and theoretical (Krishnan, Guha, and Banerjee, *Phil. Trans.*, 1933, **231**, 235; Krishnan and Banerjee, *ibid.*, 1935, **234**, 265; Pauling, *J. Chem. Physics*, 1936, **4**, 673; Lonsdale, *Proc. Roy. Soc.*, 1937, *A*, **159**, 149; London, *J. Physique*, 1937, **8**, 397), of the diamagnetic anisotropy of various aromatic molecules have shown that the degree of conjugation of the molecular framework is closely connected with the magnitude of the anisotropy. Systems containing large or numerous conjugated rings have a large diamagnetic susceptibility perpendicular to the plane of the ring, whereas normal aliphatic molecules have small anisotropies. Octahydrochrysene is found to have the same anisotropy as naphthalene (Lonsdale, *loc. cit.*), indicating that the *cyclo*hexane ring is nearly isotropic. The presence of conjugation, or resonance, even without a closed ring structure, is accompanied by high anisotropy; *e.g.*, the carbonate radical $CO_3^{--}$, which is known to have trigonal symmetry (Ewald and Hermann, "Strukturbericht," 1931, p. 317; Pauling, Brockway, and Beach, *J. Amer. Chem. Soc.*, 1935, **57**, 2706; Sidgwick, "The Organic Chemistry of Nitrogen," 1937, Introduction, p. xvii) and must therefore be a combination of the systems (I), (II), and (III), has an anisotropy of

(I.) 


(II.) 


(III.) 


$4{\cdot}0 \rightarrow 5{\cdot}0 \times 10^{-6}$ (Krishnan, Guha, and Banerjee, *loc. cit.*), and so has $NO_3^-$, whereas that of the sulphate and the selenate group, which have a tetrahedral structure, is only about $0{\cdot}75 \times 10^{-6}$. Such conjugated systems are also plane, or tend to be plane even when opposed by considerable distorting forces (Clews and Lonsdale, *Proc. Roy. Soc.*, 1937, *A*, **161**, 493; Lonsdale, *Z. Krist.*, 1936, **95**, 471).

The existence of large anisotropy in a diamagnetic crystal is therefore presumptive evidence of (*i*) molecular conjugation, (*ii*) the arrangement of atoms (or the tendency of atoms to arrange themselves) in sheets normal to the direction of greatest numerical diamagnetic susceptibility.

Most of the studies hitherto carried out have concerned derivatives of benzene and cyanuric rings. The author has now measured the principal susceptibilities of metal-free phthalocyanine, oxalic acid dihydrate, stilbene, tolan, and *trans*-azobenzene, all of which have been (or are being) subjected to a complete *X*-ray analysis.

## Experimental.

*Metal-free Phthalocyanine*, $C_{32}H_{18}N_8$.—Preliminary measurements of the magnetic aniso tropy of this substance gave $(\chi_2 - \chi_1)_{mol.} = -372 \pm 18$, $(\chi_3 - \chi_1)_{mol.} = -397 \pm 40$ (th factor $10^{-6}$ is omitted in this and all succeeding data). The best single crystals were used fo the measurements of anisotropy, and since they were rather fragile, they did not survive th part of the investigation. Those that remained weighed less than 0·1 mg., and therefore

modification of Krishnan's "suspension method" (Krishnan and Banerjee, *Current Sci.*, 1935, **3**, 548) was used for the measurement of absolute susceptibility. The crystal density was 1·445 g./c.c. at 20°; two solutions of this density were made up, one of strontium bromide (more diamagnetic), the other of this salt together with nickel chloride (less diamagnetic than the estimated value of the minimum crystal susceptibility). In a suitable mixture of these two, the crystals merely orientated themselves without any tendency to move laterally when the magnetic field was imposed. The crystals and solution were contained in a thin-walled glass tube, which could be suitably closed to prevent evaporation, and then suspended from one arm of a sensitive balance. By arranging that the lower part of the tube should be in a uniform field of about 8000 gauss, and the upper part in a negligible field, while the gradient was as large as possible over a region of 3 mm. at the edge of the pole-pieces, the behaviour of the crystals within this gradient could be observed and the susceptibility of the surrounding liquid measured almost simultaneously by the Gouy method. Distilled water was used as a standard, and this was checked by measurement of the susceptibilities of water-free methyl and ethyl alcohols. On the assumption that $\chi_{H_2O} = -0{\cdot}720$ and $\kappa_{air} = +0{\cdot}029$ at 20°, the method gave $\chi_{MeOH} = -0{\cdot}677 \pm 0{\cdot}004$, and $\chi_{EtOH} = -0{\cdot}733 \pm 0{\cdot}004$, at 21°, as compared with Cabrera and Fahlenbrach's values (*Z. Physik*, 1933, **85**, 568), $\chi_{MeOH} = -0{\cdot}6743 \pm 0{\cdot}0036$ at 19·8°, and $\chi_{EtOH} = -0{\cdot}7324 \pm 0{\cdot}0024$ at 20°. Since the temperature dependence of $\chi$ in these cases is negligible, the agreement was very satisfactory.

Owing to the very small size and lath-like shape of the phthalocyanine crystals, together with their high density, the method was not capable of giving very accurate results. The solutions were rather viscous, and convection currents set up by changes of temperature had to be avoided. The possible error with the most intense gradient available was estimated at about $\pm$ 5%, taking the mean of several separate determinations. The measurement of absolute susceptibility was made along $\chi_1$, which is inclined at 47·5° to the *c* axis in the obtuse angle $\beta$; $\chi_1 = -166 \pm 8$, hence $\chi_2 = -538 \pm 26$, normal to $\chi_1$ in (010), and $\chi_3 = -563 \pm 48$, along [010].

*Oxalic Acid Dihydrate.*—Most of the measurements were made on a large fine crystal weighing 24·63 mg., *d* 1·615 g./c.c. at 20°. The absolute susceptibility was measured by the Rabi–Krishnan method (Krishnan, Guha, and Banerjee, *loc. cit.*), but since oxalic acid reacts with most salts, a mixture of water and glycerol, both previously saturated with oxalic acid, was used. This gave $\chi_1 = -53{\cdot}1 \pm 0{\cdot}5$. Measurements of anisotropy, using *s*-triphenylbenzene ($\chi_c - \chi_a = -173$) as a standard, gave $\chi_2 - \chi_1 = -1{\cdot}91, \chi_3 - \chi_1 = -7{\cdot}05, \chi_3 - \chi_2 = -5{\cdot}14$. Hence $\chi_1 = -53{\cdot}1 \pm 0{\cdot}5$, $\chi_2 = -55{\cdot}01$, normal to $\chi_1$ in (010), $\chi_3 = -60{\cdot}15$, along [010]; $\chi_1$ makes an angle of 0·6° with the *c* axis in the obtuse angle $\beta$.

*Stilbene, Azobenzene, and Tolan.*—These compounds form fine large monoclinic crystals, which are isomorphous both in habit and in structure (Robertson, Prasad, and Woodward, *Proc. Roy. Soc.*, 1936, *A*, **154**, 187). Stilbene and azobenzene are insoluble in water, but tolan proved to be slightly soluble in hot water. The absolute susceptibilities and anisotropies were measured on a number of different crystals, and consistent results were obtained, which were estimated to be correct to within 0·5%. Mean results are given in the following table, the measurement of absolute susceptibility having been made in each case on the numerically least of the three principal values (italicised).

| | *d*. | $(\chi_2 - \chi_1)$. | $(\chi_2 - \chi_3)$. | $(\chi_3 - \chi_1)$. | $\chi_1$. | $\chi_2$. | $\chi_3$. | $\psi$. |
|---|---|---|---|---|---|---|---|---|
| Stilbene ........... | 1·161 | −46·9 | −48·0 | +1·4 | −99·9 | −146·8 | *−98·8* | −66·0° |
| Tolan ............... | 1·133 | −50·9 | −49·0 | −1·4 | *−98·5* | −149·4 | −99·9 | −62·5 |
| Azobenzene ......... | 1·225 | −49·3 | −54·4 | +5·2 | −88·1 | −137·4 | *−83·0* | −65·6 |

In each case $\chi_1$ lies very close to the *a* crystallographic axis. The results for stilbene and azobenzene differ from those first reported by Krishnan, Guha, and Banerjee (*loc. cit.*), but are in agreement with later measurements (privately communicated by Professor Krishnan in reply to an enquiry).

## Discussion of Results.

*Molecule Susceptibilities.—Metal-free phthalocyanine.* Robertson has carried out a complete Fourier analysis of the structure of this compound, and gives the direction cosines of a molecule relative to the *a*, *b*, *c'* (normal to *a* and *b*) axes, as

$$\left.\begin{array}{llllll} \cos\alpha_L & 0{\cdot}3532, & \cos\beta_L & 0{\cdot}0395 & \cos\gamma_L & 0{\cdot}9347 \\ \cos\alpha_M & 0{\cdot}6615 & \cos\beta_M & 0{\cdot}6960 & \cos\gamma_M & -0{\cdot}2794 \\ \cos\alpha_N & -0{\cdot}6617 & \cos\beta_N & 0{\cdot}7169 & \cos\gamma_N & 0{\cdot}2197 \end{array}\right\} \quad . \quad . \quad (1)$$

L and M being specified directions *in* the plane of the molecule, and N normal to that plane. Relative to the $\chi_1$, $\chi_2$, $\chi_3$ axes the direction cosines of L, M, N are

$$\left.\begin{array}{llllll} \cos\theta_{L1} & 0.9951 & \cos\theta_{L2} & -0.0906 & \cos\theta_{L3} & 0.0395 \\ \cos\theta_{M1} & -0.0924 & \cos\theta_{M2} & -0.7121 & \cos\theta_{M3} & 0.6960 \\ \cos\theta_{N1} & 0.0349 & \cos\theta_{N2} & 0.6963 & \cos\theta_{N3} & 0.7169 \end{array}\right\} \quad . \quad . \quad (2)$$

This shows that the $\chi_1$ axis is only about 5° away from the L direction in the molecule; it follows therefore that the susceptibility along L ($\kappa_L$) must be very nearly equal to $\chi_1$ ($= -166$). By assuming $\kappa_L = \kappa_M$ and using the formulæ $\chi_1 = \kappa_L + \Delta\kappa . \cos^2\theta_{N1}$, $\chi_2 = \kappa_L + \Delta\kappa . \cos^2\theta_{N2}$, etc., $\kappa_2 = -166$, $\Delta\kappa = \chi_1 + \chi_2 + \chi_3 - 3\kappa_L = -769$, we obtain the following estimate of the orientation of N, the normal to the molecular plane, relative to the $\chi_1$, $\chi_2$, $\chi_3$ axes:

$$\cos\theta_{N1} = 0 \qquad \cos\theta_{N2} = 0.6956 \qquad \cos\theta_{N3} = 0.7185$$

These values are very close to those of Robertson, *viz.*,

$$\cos\theta_{N1} = 0.0347 \qquad \cos\theta_{N2} = 0.6963 \qquad \cos\theta_{N3} = 0.7169$$

If, however, the reverse process is followed and the values of the molecule susceptibilitie[s] $\kappa_L$, $\kappa_M$, $\kappa_N$ are calculated from the set of equations

$$\chi_1 = \kappa_L \cos^2\theta_{L1} + \kappa_M \cos^2\theta_{M1} + \kappa_N \cos^2\theta_{N1}, \text{ etc.}$$

we find $\kappa_L = -165$, $\kappa_M = -120$, $\kappa_N = -982$.

Alternatively, $\kappa_L$, $\kappa_M$, $\kappa_N$ can be calculated directly (see Lonsdale and Krishnan, *loc. cit.* from $\chi_1$, $\chi_2$, $\chi_3$ and $\alpha_L$, $\gamma_L$, $\alpha_M$, and hence an independent estimate of $\psi$, the angle betwee[n] $\chi_1$ and the *c* crystal axis, can be obtained. Adopting this method, we find $\kappa_L = -16$[6] $\kappa_M = -104$, $\kappa_N = -997$, $\psi = +50.2°$ (cf. observed value $+47.5°$).

Robertson's analysis showed that the molecule is plane and nearly tetragonal, in whic[h] case it seems unlikely that $\kappa_M$ should be so much less than $\kappa_L$. A little time, therefore, ha[s] been spent in investigating the dependence of the calculated values of $\kappa_M$ upon the valu[e] of the molecular direction cosines.

The angle whose cosines are given above (2) are obtained from Robertson's values, giv[en] by a Fourier analysis of the structure (J., 1936, 1195) and the directly measured value of

If we assume that one of these, say $\theta_{L1}$, is correct, and that $\kappa_L = \kappa_M = -166$, $\kappa_N =$ 935, we can calculate a set of direction cosines which will give the observed values $\chi_1$, $\chi_2$, $\chi_3$. These direction cosines are as follows:

$$\left.\begin{array}{llllll} \cos\theta_{L1} & 0.9951 & \cos\theta_{M1} & -0.0985 & \cos\theta_{N1} & 0 \\ \cos\theta_{L2} & -0.0709 & \cos\theta_{M2} & -0.7150 & \cos\theta_{N2} & 0.6956 \\ \cos\theta_{L3} & 0.0684 & \cos\theta_{M3} & 0.6922 & \cos\theta_{N3} & 0.7185 \end{array}\right\} \quad . \quad . \quad (3)$$

None of these values gives an angle differing from the former experimental result more than 2°, and six of them differ by not more than a few minutes. It follows theref that the values of $\kappa_M$ and $\kappa_N$ are closely dependent upon the accuracy of the molec[u] direction cosines, small variations in the cosines producing large variations in $\kappa_M$, although $\kappa_L$ is not much affected by small changes in these cosines. On the other ha[nd] calculations of the orientation of the molecular plane from the measured values of $\chi_1$, $\chi$[...] and estimated molecule susceptibilities $\kappa_L$, $\kappa_M$, $\kappa_N$, will be nearly correct, even if the assu[mp]tion that $\kappa_L = \kappa_M$ is far from true.

The implications of the very large anisotropy of the phthalocyanine molecule h[ave] already been discussed (Lonsdale, *Proc. Roy. Soc.*, 1937, *A*, **159**, 149).

*Oxalic acid dihydrate.* The complete *X*-ray examination of this substance by Rober[tson] and Woodward (J., 1936, 1817) showed that the molecule is plane and the C–C distan[ce in] the oxalate group is only 1·43 → 1·45 A. This indicates the presence of double-[bond] properties in this link, presumably due to the conjugation of double bonds in adja[cent] carboxyl groups. It seemed likely, therefore, that there might be a marked mole[cular] anisotropy, which could be compared with that due to the carbonate $CO_3^{--}$ group, in w[hich] there is a similar plane arrangement of atoms, with a shortening of the C–O link (El[...] *J. Amer. Chem. Soc.*, 1937, **59**, 1380).

Robertson and Woodward give the direction values of the principal directions in the oxalate group (L, M in the plane of the group, N normal to that plane). These can be combined with $\chi_1$, $\chi_2$, $\chi_3$, and $\psi$, to give $\kappa_L$, $\kappa_M$, $\kappa_N$ as before :

$$\kappa_L = -53{\cdot}13,\ \kappa_M = -52{\cdot}73,\ \kappa_N = -62{\cdot}40.$$

In this case the anisotropy is relatively small and the susceptibilities do not vary much with small changes in the direction cosines. The anisotropy is large, however, compared with that usually expected for aliphatic molecules, and is about twice the value found for the $CO_3^{--}$ group. Although the influence of the water molecules is not known, it seems probable that the anisotropy is mainly, if not entirely, due to the resonance in the oxalate group.

The diamagnetic oxalates studied by Krishnan and Banerjee (*Phil. Trans.*, 1936, *A*, **235**, 343) also showed an anisotropy more than five times as large as that of diamagnetic sulphates and selenates.

It is noteworthy that in the oxalate and the carbonate group there is no closed chain of conjugated bonds. *The presence of a closed ring is therefore not essential to the existence of abnormal diamagnetism.* One may predict a similar conjugation, with plane arrangement of atoms, tendency to equalisation of bond distances, and large anisotropy, in such compounds as maleic and fumaric acids, muconic acid, cinnamic acid, as well as in benzil, benzophenone, and in all the diphenylpolyenes, including stilbene, the discussion on which now follows.

*Stilbene.* Since $\chi_1$ lies along the *a* crystal axis, it follows that $\chi_1$, $\chi_2$, $\chi_3$ are coincident with *a*, *c'*, *b*; and since there are two independent pairs of centrosymmetrical molecules in the unit cell (Robertson and Woodward, *Proc. Roy. Soc.*, 1937, *A*, **162**, 568), we have

$$\left.\begin{aligned}\chi_1 &= \tfrac{1}{4}\,[\kappa_L\textstyle\sum_4 \cos^2\alpha_L + \kappa_M\sum_4 \cos^2\alpha_M + \kappa_N\sum_4 \cos^2\alpha_N]\\ \chi_2 &= \tfrac{1}{4}\,[\kappa_L\textstyle\sum_4 \cos^2\gamma_L + \kappa_M\sum_4 \cos^2\gamma_M + \kappa_N\sum_4 \cos^2\gamma_N]\\ \chi_3 &= \tfrac{1}{4}\,[\kappa_L\textstyle\sum_4 \cos^2\beta_L + \kappa_M\sum_4 \cos^2\beta_M + \kappa_N\sum_4 \cos^2\beta_N]\end{aligned}\right\} \quad . \quad . \quad . \quad . \quad (4)$$

Robertson and Woodward have given the following data for the molecular direction cosines, relative to the *a*, *b*, *c* axes.

| | | | | | | |
|---|---|---|---|---|---|---|
| Molecules 1 and 3 | $\cos\alpha_L$ | 0·8352 | $\cos\alpha_M$ | − 0·4190 | $\cos\alpha_N$ | − 0·3563 |
| | $\cos\beta_L$ | ± 0·1748 | $\cos\beta_M$ | ± 0·8187 | $\cos\beta_N$ | ∓ 0·5469 |
| | $\cos\gamma_L$ | 0·5219 | $\cos\gamma_M$ | 0·3939 | $\cos\gamma_N$ | 0·7567 |
| Molecules 2 and 4 | $\cos\alpha'_L$ | 0·8533 | $\cos\alpha'_M$ | − 0·3076 | $\cos\alpha'_N$ | − 0·4212 |
| | $\cos\beta'_L$ | ∓ 0·0278 | $\cos\beta'_M$ | ± 0·8333 | $\cos\beta'_N$ | ± 0·5521 |
| | $\cos\gamma'_L$ | − 0·5208 | $\cos\gamma'_M$ | − 0·4595 | $\cos\gamma'_N$ | − 0·7194 |

Substituting in (4), we obtain the equations

$$\begin{aligned}-\ 99{\cdot}9 &= 0{\cdot}7127\kappa_L + 0{\cdot}1348\kappa_M + 0{\cdot}1525\kappa_N\\ -146{\cdot}8 &= 0{\cdot}2717\kappa_L + 0{\cdot}1828\kappa_M + 0{\cdot}5455\kappa_N\\ -\ 98{\cdot}8 &= 0{\cdot}0156\kappa_L + 0{\cdot}6824\kappa_M + 0{\cdot}3020\kappa_N\end{aligned}$$

whence $\kappa_L = -85{\cdot}8,\ \kappa_M = -50{\cdot}1,\ \kappa_N = -209{\cdot}6.$

This result is somewhat unexpected, showing as it does a big anisotropy in the plane of the molecule. Nor is it possible, as it was with phthalocyanine, to remove the difference between $\kappa_L$ and $\kappa_M$ by a relatively small adjustment of the direction cosines. For if $\kappa_L = \kappa_M$, the first and the last equation reduce to

$$\begin{aligned}-99{\cdot}9 &= \kappa_L + 0{\cdot}1525\,(\kappa_N - \kappa_L)\\ -98{\cdot}8 &= \kappa_L + 0{\cdot}3020\,(\kappa_N - \kappa_L)\end{aligned}$$

No reasonable values of $\kappa_L$, $\kappa_N$ will satisfy these equations; the difference between $\kappa_L$ and $\kappa_M$ is, in fact, implied by the difference between $\alpha_N$ and $\beta_N$, $\chi_1$ and $\chi_3$ being nearly equal. A difference of approximately 2° in each of $\alpha_N$, $\beta_N$ (in order to make them more

nearly equal) corresponds to values of $\overline{\alpha_N^2} = 0{\cdot}1790$, $\overline{\beta_N^2} = 0{\cdot}2755$, and gives $\kappa_L = -79$, $\kappa_M = -55$, $\kappa_N = -211$. The equality of $\kappa_L$, $\kappa_M$ would therefore involve a highly improbable degree of inaccuracy both in the magnetic measurements and in the *X*-ray results. The cause of this large anisotropy in the plane of the molecule is obscure; it is worth noting, however, that in every case of a condensed or polyphenyl compound so far examined the susceptibility along the "length" of the molecule is greater than that along the "width" (Lonsdale and Krishnan, *loc. cit.*).

The values $\kappa_L = -86$, $\kappa_M = -50$, $\kappa_N = -210$ lead to an anisotropy $-124 < \Delta\kappa < -160$ (numerically). This is numerically greater than the value $-118{\cdot}6$ found for diphenyl, as might have been expected, for the chain between the phenyl groups is conjugated and will itself contribute to the anisotropy. Robertson and Woodward have found the values 1·33 A., 1·45 A. for the lengths of the "double" and "single" bonds respectively, indicating a degree of resonance about equivalent to that of the C–C bond in the oxalate group.

*Tolan.* A similar calculation for tolan, unpublished *X*-ray data being used for the direction cosines, very kindly given to me by Dr. Robertson and Miss Woodward, leads to molecule susceptibilities $\kappa_L = -81{\cdot}5$ (along length of molecule), $\kappa_M = -67{\cdot}8$ (normal to L, in plane of molecule), $\kappa_N = -198{\cdot}5$ (normal to plane of molecule). Here again the anisotropy *in* the plane of the molecule, though not as large as that of stilbene, is too large to be explained away by experimental inaccuracy. The anisotropy normal to the molecular plane, $-117 < \Delta\kappa < -131$, is of the same order as that of diphenyl.

trans-*Azobenzene.* The data for the molecular direction cosines of azobenzene are not yet available, although an *X*-ray analysis is in progress. The substitution of nitrogen for carbon atoms in the interphenyl chain has resulted in an all-round lowering of susceptibilities by about twelve units.

Davy Faraday Laboratory, London, W. 1. [*Received, November 29th, 1937.*]

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## 74. *The Stereochemistry of Metallic Derivatives of Pyrromethenes.*

By Charles R. Porter.

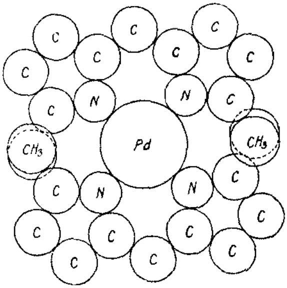
The stereochemistry of the 4-covalent metallic derivatives of pyrromethenes is discussed, and it is shown on theoretical grounds that a planar configuration is impossible for simple salts of the type $R_2M$, where RH is the pyrromethene. Typical pyrromethene derivatives of cobalt, nickel, copper, zinc, cadmium, and palladium are described. These metals therefore must be able to take up a non-planar configuration. A number of other bivalent metals are shown not to form derivatives under similar conditions.

During the last few years, evidence in favour of a planar configuration of the valencie of the metallic atoms in 4-covalent compounds has been increasing, and the work c Linstead and his co-workers on the metallic derivatives of the phthalocyanines has show that a large number of bivalent metals, many of which have normally a tetrahedral valenc distribution, can take up a planar configuration when attached to the four nitrogen aton of the phthalocyanine molecule. It was thought, however, that this molecule may impo: a constraint on the valency distribution of the metals in question, and it would appe: interesting to discover whether metals which normally give 4-covalent compounds planar type could be constrained by the use of suitable chelate groups to give 4-covale molecules of non-planar type.

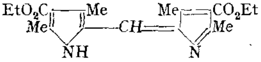
The pyrromethenes afford such a chelate group, and have the advantage, for th comparison, of being very similar to the porphyrins and phthalocyanines except in th requirement of a tetrahedral symmetry on the part of the metallic atom. Inspection a model or diagram of pyrromethene derivatives of bivalent metals shows that if all t α-positions of the base are substituted the molecule cannot have a planar configuration, that such compounds should be resolvable, and a comparison of the rates of mutarotati of these substances with those of similar derivatives containing either or both of t

α-positions unsubstituted should be of interest. A study of the pyrromethene derivatives of the metals has therefore been started with this end in view, and preliminary results are now described.

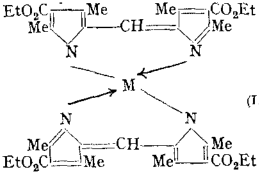
The palladium derivative of 5 : 5′-dimethylpyrromethene is shown in the diagram. The angles between the valencies of the metal have been made equal to 90°, and the sizes of the atoms are Pd = 1·37, N = 0·66, C in ring = 0·72, C in methyl group = 0·77A.; these values approximate to a mean of those found by Robertson and Woodward (J., 1937, **219**) for the phthalocyanines, except that the methyl groups have been given the dimensions usual for aliphatic carbon atoms. It will be seen that the methyl groups completely overlap, and in the case of a smaller metallic atom, such as nickel, the overlapping covers part of the nuclear carbon atom as well. The case is thus somewhat similar to that of the 2 : 2′-disubstituted diphenyl derivatives.




The most readily available pyrromethene is ethyl 3 : 3′ : 5 : 5′-tetramethylpyrromethene-4 : 4′-dicarboxylate (I). The ferrous salt of this base has been prepared by Fischer and Klarer (*Annalen*, 1926, **448**, 190), and the nickel, cobalt, copper, and zinc salts are described by Fischer and Schubert (*Ber.*, 1924, **57**, 611). The *cadmium* salt has now been prepared. The substances are readily obtained by the action of the acetates of the metals on the organic base, the reaction being always accompanied by a reddening of the colour of the solution. All these substances are of the type $R_2M$ where RH is the base (II).



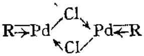

(I.)



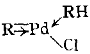

(II.)

With palladium, more complex results were obtained. In the presence of excess potassium chloropalladite, and sodium acetate in aqueous alcoholic solution, the pyrromethene gave a mixture of products from which was isolated the bimolecular compound, *bis-(4 : 4′-dicarbethoxy-3 : 3′ : 5 : 5′-tetramethylpyrromethene)dipalladous dichloride*, $R_2Pd_2Cl_2$, and the monopalladous *chloride*, $R_2HPdCl$. (The exact number of hydrogen atoms in this molecule is not determinable by elementary analysis, but a change of valency of palladium is unlikely.) The former substance was transformed into the latter on treatment in alcoholic solution with two molecular proportions of the base.

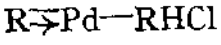
The bimolecular substance, $R_2Pd_2Cl_2$, presumably has the structure (III), and could




(III.)



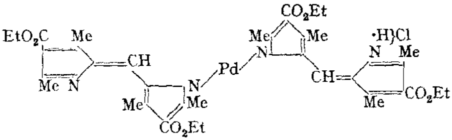

(IV.)




(V.)

possibly assume a planar configuration. The unimolecular compound might possibly be either (IV) or (V). The latter formulation is very unsatisfactory, for a co-ordination number of 3 is unlikely for palladium; in neither case could the palladium atom have a planar configuration unless neighbouring but not mutually attached carbon atoms approach

much closer than is usually supposed possible. In the formulation, R—Pd—RHCl, a planar configuration is possible if the pyrrole rings are rotated about the single bonds joining them to the bridge carbon atom (VI). The substance is not very stable, and



(VI.)

even on boiling with alcohol, the elements of hydrogen chloride are removed with the formation of *bis-(4 : 4'-dicarbethoxy-3 : 3' : 5 : 5'-tetramethylpyrromethene)palladium*, $R_2Pd$. A good yield of this compound could also be obtained directly by the action of one equivalent of palladous nitrate on the base in the presence of sodium acetate. In distinction from the previously described derivatives of pyrromethenes, the palladium derivative is microcrystalline and almost insoluble in the common solvents except chloroform; it is, however, unimolecular and is therefore presumably of the non-planar type.

The difference in the reactions of palladium nitrate and potassium chloropalladite with this base is presumably due to the fact that $Pd^{++}$ ions are not present to any appreciable extent in the latter case.

Somewhat similar results were observed when mercuric chloride was used. With excess of this, the pyrromethene gave an almost quantitative deposition of a *product* having the empirical formula, RHgCl. When the sulphate or nitrate was used, the result depended on the amount of reagent employed. With excess of either inorganic reagent dissolved in excess aqueous acetic acid, an alcoholic solution of the base gave an almost quantitative precipitation of a *compound* of the formula RHgOAc. When one molecular proportion of the pyrromethene was treated with one equivalent of mercuric nitrate, however, a *compound* of the normal type, $R_2Hg$, was obtained. On the other hand, when the pyrromethene was treated with one equivalent of mercuric chloride, only half of the base reacted, forming the chloro-compound previously mentioned.

The bivalent ions of beryllium, magnesium, chromium, manganese, and lead do not appear to form derivatives with this pyrromethene under similar conditions.

For comparison, metallic derivatives of the corresponding pyrromethene with free α-positions have been prepared. In compounds of this type, the α-carbon atoms should not touch, but should nevertheless approach closer, if a planar configuration be assumed, than is usual for carbon atoms not directly linked to one another. Ethyl 3 : 3'-dimethylpyrromethene-4 : 4'-dicarboxylate is distinctly less stable than the fully substituted substance, and metallic derivatives are best prepared by the addition of the calculated amount of the acetate to a cold alcoholic solution of the base. The salts are microcrystalline.

All the metallic derivatives described are insoluble in water, but are soluble in chloroform, those of smaller molecular weight being also soluble in benzene. The genera properties of the substances suggest that the organic bases attach themselves to the metal as chelate groups, although the compound $R_2HPdCl$ is difficult to formulate on thi assumption. Schmitz and Dumont (*Ber.*, 1929, **62**, 226) obtained a compound of the typ $RHSnCl_4$, and suggested that the pyrromethene occupies two co-ordination positions The corresponding pyrromethanes neither form derivatives with metals nor readily forr salts with acids.

The pyrromethene residues are not so firmly attached to the metals, except in the cas of mercury and palladium, as are the porphyrins and phthalocyanines, the metal beir eliminated in the case of nickel and copper by the action of 3N-hydrochloric acid. C being heated in air, the compounds decompose, leaving quantitative residues of the meta or their oxides.

## EXPERIMENTAL.

Ethyl 3 : 3′ : 5 : 5′-tetramethylpyrromethene-4 : 4′-dicarboxylate was prepared by the method of Fischer, Werner, and Zerweck (*Ber.*, 1923, **56**, 526), and the 3 : 3′-dimethyl analogue by that of Fischer and Wiedemann (*Z. physiol. Chem.*, 1926, **155**, 52).

*Metallic Derivatives of Ethyl Tetramethylpyrromethene*-4 : 4′-*dicarboxylate*.—The cobalt, nickel, cupric, zinc, and cadmium compounds were prepared by warming an alcoholic solution of the base or its hydrochloride with excess of a concentrated aqueous solution of the acetate of the metal or the corresponding chloride mixed with sodium acetate. The solution reddened when the reagents were mixed, and after ½ hour the complex salts were precipitated by the addition of water. They were purified by recrystallisation from chloroform–petrol and from alcohol. They do not show sharp m. p.'s, but decompose over a range depending somewhat on the rate of heating.

The cobalt, nickel, copper, and zinc salts were prepared as described by Fischer and Schubert (*loc. cit.*). The cobalt salt had $M = 751$ in freezing benzene and the copper salt $M = 670$ in freezing bromoform (Calc.: $M = 745$ and 750 respectively). The *cadmium* derivative, brick red, sinters and decomposes at 235—245°; it is rather less soluble than the above compounds, being sparingly soluble except in chloroform, and was recrystallised from acetone (Found: Cd, 14·35. $C_{38}H_{46}O_8N_4Cd$ requires Cd, 14·1%).

*Palladium derivatives*. The pyrromethene (0·45 g., 1 mol.) and sodium acetate (1 mol.) were dissolved in alcohol, and potassium chloropalladite (1·6 mol.), dissolved in water, was added together with sufficient of the solvents to keep the reagents in solution in the cold. The colour gradually darkened, and after a day, 0·14 g. of reddish-brown crystalline powder (A) was removed. The alcoholic filtrate was treated with water, depositing a further 0·35 g. of product (B). The filtrate from this contained uncrystallisable material soluble in chloroform and containing palladium. (B) was left in contact with acetone for a day, and filtered, giving an insoluble portion (C), 0·18 g., and a soluble portion (D). The substance (C), recrystallised from chloroform–petrol, separated as brownish-red felted masses or as nearly black separate crystals decomposing at 235° [Found: C, 47·15; H, 5·1; Pd, 21·7; Cl, 7·55; $M$ (cryoscopic in bromoform), 926. $C_{38}H_{46}O_8N_4Pd_2Cl_2$ requires C, 47·0; H, 4·8; Pd, 22·0; Cl, 7·3%; $M$, 971]. The material (A) was triturated with acetone, in which it was almost insoluble, and recrystallised in the cold from chloroform–petrol. This bright red *substance* was much more soluble than the previous compound, and decomposed indefinitely at 170—200°. It could be prepared from the compound $R_2Pd_2Cl_2$ by warming it in alcohol with two molecular proportions of the parent pyrromethene, and precipitating with petrol [Found: C, 54·7; H, 5·9; Pd, 12·85; Cl, 4·5; $M$ (cryoscopic in benzene), 765. $C_{38}H_{47}O_8N_4PdCl$ requires C, 54·95; H, 5·7; Pd, 12·85; Cl, 4·3%; $M$, 830]. On prolonged boiling with alcohol, a less soluble substance separated, but this could be much more easily prepared by triturating in alcohol with silver carbonate or oxide, in which case a theoretical yield could be obtained. This derivative is a microcrystalline brick-red powder, decomposing at 322°, almost insoluble in the usual solvents except chloroform, from which it is best purified by precipitation with alcohol. It may also be prepared in 67% yield by the addition of palladous nitrate (1 mol.), dissolved in water, to the base (2 mols.) with excess of sodium acetate in alcohol [Found: C, 57·7; H, 6·1; Pd, 13·1, 13·5; $M$ (cryoscopic in bromoform), 792. $C_{38}H_{46}O_8N_4Pd$ requires C, 57·5; H, 5·85; Pd, 13·45%; $M$, 793]. The *substance* may be precipitated unchanged by the dilution of its solution in concentrated sulphuric acid.

*Mercuric derivatives*. On the addition of excess mercuric chloride to the base with sodium acetate in alcohol, an almost quantitative yield of an orange microcrystalline halogen-containing substance is precipitated. With only one equivalent of mercuric chloride, only half the base is precipitated. The *product* is almost insoluble in the usual solvents, sparingly soluble in chloroform, and was recrystallised from bromoform; it sinters and melts at 214—216° (Found: C, 39·0; H, 4·2; Hg, 34·0; Cl, 6·2. $C_{19}H_{23}O_4N_2HgCl$ requires C, 39·35; H, 4·0; Hg, 34·6; Cl, 6·1%).

When excess mercuric nitrate or sulphate dissolved in hot dilute aqueous acetic acid was added to an alcoholic solution of the pyrromethene under similar conditions, an almost quantitative amount of orange microcrystalline material was precipitated after a few moments. This *substance* is more soluble than the above, and may be recrystallised from acetone or chloroform–petrol. Although individual crystals are minute, the substance on crystallising appears to fill the whole volume of the solution until pressed down; m. p. 217—220° (decomp.) (Found: C, 41·6; H, 4·5; Hg, 32·9, 32·85. $C_{21}H_{26}O_6N_2Hg$ requires C, 41·8; H, 4·35; Hg, 33·3%).

Mercuric nitrate (1 equiv.), dissolved in water containing the minimal amount of nitric or acetic acid necessary for solution, was added to an alcoholic solution of the pyrromethene. The solution darkened, and a quantitative precipitation of an orange *product* was formed; recrystallised from acetone and chloroform–petrol, this had m. p. 227—230° (decomp.) (Found: C, 51·2; H, 5·4; Hg, 22·2. $C_{38}H_{46}O_8N_4Hg$ requires C, 51·4; H, 5·2; Hg, 22·6%).

The action of other bivalent metals on this pyrromethene was investigated by treating it in alcoholic solution with beryllium, magnesium, chromous, manganous, and plumbous acetates. No change in colour was observed on mixing the reagents, and the base could be recovered unchanged after the reaction. Neither were complex salts formed by the action of the pyrromethene on the freshly precipitated hydroxides or carbonates of these metals. On prolonged boiling with these reagents the colour darkened owing to deomposition of the pyrromethene.

*Metallic Derivatives of Ethyl* 3 : 3'-*Dimethylpyrromethene*-4 : 4'-*dicarboxylate*.—The cobalt, nickel, copper, zinc, and cadmium compounds were prepared by the addition of the acetates of these metals in very slight excess to a cold alcoholic solution of the base. The products were more unstable and less soluble than those of the fully methylated compound. *Cobalt* salt, m. p. 340° (decomp.) (Found: Co, 8·3. $C_{34}H_{38}O_8N_4Co$ requires Co, 8·55%). *Nickel* salt, m. p. 315° (decomp.) (Found: Ni, 8·4. $C_{34}H_{38}O_8N_4Ni$ requires Ni, 8·5%). *Copper* salt, m. p. 305° (decomp.) (Found: Cu, 9·05. $C_{34}H_{38}O_8N_4Cu$ requires Cu, 9·15%). *Zinc* salt, m. p. 302° (decomp.) (Found: Zn, 9·3. $C_{34}H_{38}O_8N_4Zn$ requires Zn, 9·4%). *Cadmium* salt, m. p. 316° (decomp.) (Found: Cd, 15·35. $C_{34}H_{38}O_8N_4Cd$ requires Cd, 15·15%).

The author's thanks are due to Professor W. Wardlaw for advice and encouragement.

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## 75. *Derivatives of* 1 : 2 : 3 : 4-*Tetrahydroxybenzene. Part IV. Attempted Syntheses.*

By WILSON BAKER and (MISS) C. EVANS.

The paper describes a number of compounds which were made with the ultimate object of synthesising derivatives of 1 : 2 : 3 : 4-tetrahydroxybenzene. Investigation of the properties of these compounds, however, showed that they could not be used as intermediates in the production of substances of the desired type.

SEVERAL methods for the synthesis of naturally occurring derivatives of 1 : 2 : 3 : 4 tetrahydroxybenzene, in particular parsley apiole and fraxetin, have been explored. Th compounds described in this paper were prepared as intermediates, but their propertie were such as to render them useless for the object in view. We have not considered i necessary to record the proposed steps of any of the synthetical schemes.

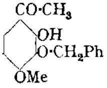
The sodium salt of 2 : 5-*dimethoxybenzenesulphonic acid* could not be converted int 2 : 5-dimethoxyphenol by fusion with caustic alkalis, the only isolable product bein quinol dimethyl ether. The sulphonic acid group is extremely easily eliminated from th acid; its dihydrate undergoes rapid hydrolysis to sulphuric acid and quinol dimeth ether at 150°.

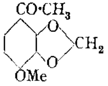
2 : 5-Dimethoxyaniline yielded only minute traces of unrecognisable phenolic materi when diazotised under a layer of light petroleum to prevent frothing (cf. Perkin an Rubenstein, J., 1926, 360), and decomposed by pouring into a boiling copper sulpha solution. Other methods of decomposing the diazonium solution were equally unsuccessf

Pyrogallol 1-monomethyl ether was converted by the method of Gattermann in 2 : 3-*dihydroxy*-4-*methoxybenzaldehyde*. This compound was unattacked by hydrog peroxide under the usual conditions of the Dakin reaction, and the same inertness w shown by 2 : 3-dihydroxy-4-methoxyacetophenone (Baker, Jukes, and Subrahmanya J., 1934, 1683). The position assigned to the aldehyde group is based on analogy with t position taken up by the acetyl group when introduced into the nucleus of pyrogal 1-monomethyl ether. Benzylation of 2 : 3-dihydroxy-4-methoxyacetophenone yield 2-*hydroxy*-3-*benzyloxy*-4-*methoxyacetophenone* (I); attempts to oxidise this to a catec

derivative by means of the Dakin reaction were unsuccessful, and the oxidation which occurred was accompanied by the production of benzyl alcohol.

2 : 4-Dihydroxyanisole (convenient preparation of the intermediate 5-amino-2-methoxyphenyl acetate) was converted into *7-hydroxy-6-methoxy-4-methylcoumarin* (*4-methylscopoletin*) by the action of acetoacetic ester and sulphuric acid, and the related *acetyl* derivative yielded *7-hydroxy-6-methoxy-8-acetyl-4-methylcoumarin* when heated with aluminium chloride. Hydrolysis of this compound gave, not the desired 2 : 4-dihydroxy-3-acetylanisole, but 2 : 4-dihydroxyanisole.


(I.)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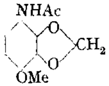
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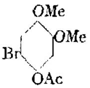
(IV.)

Treatment of 2 : 3-dihydroxy-4-methoxyacetophenone with methylene sulphate and alkali gave *4-methoxy-2 : 3-methylenedioxyacetophenone* (II), the *oxime* of which was converted into *4-methoxy-2 : 3-methylenedioxyacetanilide* (III) by the action of phosphorus pentachloride in ether. The corresponding free amine gave some indications of being converted into a quinone on oxidation (cf. oxidation of 2 : 3 : 4-trimethoxyaniline to 2 : 3-dimethoxy-*p*-benzoquinone; Baker and Smith, J., 1931, 2547), but the small amount of material available was insufficient for a complete investigation of the reaction.

4-Hydroxyveratrole (considerably improved preparation from 4-aminoveratrole) was converted into *5-bromo-4-acetoxyveratrole* (IV) (1) by bromination, followed by acetylation, (2) by conversion into *4-acetoxyveratrole* and subsequent bromination, the latter method being the better. Attempts to effect the migration of the acetyl group in (IV) into position 3 by treatment with aluminium chloride under various conditions, or to introduce a new acetyl group into position 3 by the action of acetic acid and zinc chloride or acetic anhydride and sulphuric acid (Schneider and Kraft, *Ber.*, 1922, **55**, 1892) were unsuccessful. Position 3 appears to be very unreactive and vigorous conditions lead to decomposition. 5-Bromo-1 : 2 : 4-trimethoxybenzene, when treated with acetyl chloride and aluminium chloride under various conditions, gave, not a nuclear acetyl derivative, but 2 : 3 : 5 : 2′ : 3′ : 5′-hexamethoxydiphenyl, which was also produced under the same conditions in the absence of acetyl chloride.

## Experimental.

2 : *5-Dimethoxybenzenesulphonic Acid*.—This acid has been referred to by Hantzsch and Langbein (*Z. anorg. Chem.*, 1932, **204**, 193), but no description of the acid or of its preparation occurs in the literature, apart from the statement by Hantzsch and Langbein that, after drying at 100° in air, it contains $1H_2O$. We find, however, that under these conditions the acid contains $2H_2O$.

Quinol dimethyl ether (100 g.) and concentrated sulphuric acid (200 c.c.) were warmed at 60° for 5 minutes (slight exothermic reaction), and after 10 minutes water (400 c.c.) was added, and the solution cooled. After several hours the crystals were collected, drained, and dried as far as possible over sulphuric acid (weight, 174 g.). 2 : *5-Dimethoxybenzenesulphonic acid* crystallises from ethyl acetate in large, highly refracting bi-pyramids or elongated prisms. The crystals become slightly opaque on the surface on standing or on heating to 100° (Found in material powdered and heated at 100° : C, 37·7; H, 5·3; S, 12·5; equiv., 257. $C_8H_{10}O_5S,2H_2O$ requires C, 37·8; H, 5·5; S, 12·6%; equiv., 254). The acid dissolves in its water of crystallisation at 100—105°.

2 : *3-Dihydroxy-4-methoxybenzaldehyde*.—To pyrogallol 1-methyl ether (10 g.) (Baker, Montgomery, and Smith, J., 1932, 1282; Baker, Jukes, and Subrahmanyam, *loc. cit.*) in dry ether (100 c.c.) was added anhydrous zinc cyanide (6·8 g.) and a rapid current of dry hydrogen chloride passed in with vigorous stirring until the cyanide had dissolved. After 1½ hours the ether was decanted from the crystalline solid, the latter boiled with water for 10 minutes, and the solution extracted several times with ether. After drying and distilling, the extracts yielded the *aldehyde* as a colourless solid, m. p. 69·5°, b. p. 172—178°/14 mm. (Found: C, 57·1; H, 5·0. $C_8H_8O_4$ requires C, 57·1; H, 4·8%).

*2-Hydroxy-3-benzyloxy-4-methoxyacetophenone* (I).—2 : 3-Dihydroxy-4-methoxyacetophenone (10 g.) (Baker, Jukes, and Subrahmanyam, *loc. cit.*) in dry toluene (750 c.c.) was boiled under reflux with continual stirring in presence of anhydrous potassium carbonate (110 g.), and benzyl chloride (60 g.) added at intervals during 9 hours. Water was now added, the toluene removed in steam, and the residue, which solidified, crystallised from light petroleum (b. p. 60—80°). The *benzyl* derivative separates from this solvent or methyl alcohol in colourless needles, m. p. 79—80° (Found: C, 70·8; H, 5·9. $C_{16}H_{16}O_4$ requires C, 70·7; H, 5·9%). Yield, 40%. Its alcoholic solution gives a deep purplish-brown colour on the addition of ferric chloride. The position of the benzyl group is established by the fact that hydroxyl ortho to a carbonyl group cannot be benzylated under the normal conditions (Gulati and Venkataraman, J., 1936, 267).

*5-Amino-2-methoxyphenyl Acetate.*—This intermediate in the preparation of 2 : 4-dihydroxyanisole was most conveniently prepared by the catalytic reduction of the corresponding nitro-compound (cf. Seka and Kallir, *Ber.*, 1931, 64, 913). 5-Nitro-2-methoxyphenyl acetate (40 g.) in alcohol (150 c.c.) was shaken in hydrogen under 3 atms. pressure in presence of a palladium–strontium carbonate catalyst (7·5 g.; from 50 g. of strontium carbonate and 1 g. of palladium chloride) till reduction was complete (about 2 hours). The free amine was obtained by evaporation of the filtered solution and was used directly in the diazonium reaction. *5-Acetamido-2-methoxyphenyl acetate* separated from hot water in glistening plates, m. p. 156—157° (Found: C, 59·1; H, 5·7; N, 6·3. $C_{11}H_{13}O_4N$ requires C, 59·2; H, 5·8; N, 6·3%).

2 : 4-*Dihydroxyanisole.*—This was prepared directly from 5-amino-2-methoxyphenyl acetate, simultaneous hydrolysis of the acetoxy-group occurring. Decomposition of the diazonium sulphate was effected by pouring into a boiling copper sulphate solution (cf. preparation of 4-hydroxyveratrole; p. 375), and the 2 : 4-dihydroxyanisole isolated in 52% yield, following the directions given by Seka and Kallir (*loc. cit.*), who prepared it from 5-amino-2-methoxyphenol.

*7-Hydroxy-6-methoxy-4-methylcoumarin* (*4-Methylscopoletin*).—A mixture of 2 : 4-dihydroxyanisole (7·5 g.) and acetoacetic ester (5·5 g.) was added to concentrated sulphuric acid (25 g.) at 0°. After 12 hours the solution was poured on ice, and the precipitate collected, washed, and crystallised from dilute alcohol. The *coumarin* separated in minute prisms, m. p. 213·5° (Found: C, 64·1; H, 4·8. $C_{11}H_{10}O_4$ requires C, 64·1; H, 4·8%). Its solutions in water, alcohol, and concentrated sulphuric acid possess marked blue fluorescence. The ferric chloride reaction is green, and the solution in sodium hydroxide is yellow with a strong blue fluorescence. The *acetyl* derivative, prepared by refluxing with acetic anhydride for ½ hour, forms colourless, prismatic needles from methyl alcohol, m. p. 188—189° (Found: C, 62·7; H, 5·1. $C_{13}H_{12}O_5$ requires C, 63·0; H, 4·9%).

*7-Hydroxy-6-methoxy-8-acetyl-4-methylcoumarin.*—The foregoing acetyl derivative (2 g.) was mixed with powdered aluminium chloride (4 g.) and placed in an oil-bath at 120°, the temperature being raised to 170° during 1½ hours. The product was decomposed with dilute hydrochloric acid, and the resulting solid crystallised twice from alcohol (charcoal) and then from dilute alcohol. It formed very pale yellow needles, m. p. about 250° (decomp. and previous softening) (Found: C, 63·0; H, 4·6. $C_{13}H_{12}O_5$ requires C, 63·0; H, 4·9%). The compound is only sparingly soluble in cold sodium hydroxide to an intensely yellow solution with a slight blue-green fluorescence, the weakly phenolic character being consistent with the position assigned to the acetyl group. The alcoholic solution is coloured a deep olive-green by the addition of ferric chloride.

*4-Methoxy-2 : 3-methylenedioxyacetophenone* (II).—2 : 3-Dihydroxy-4-methoxyacetophenone (5 g.) in dry acetone (200 c.c.) was stirred (mercury seal) and boiled under reflux in an atmosphere of coal gas, a solution of potassium hydroxide (10 g.) in water (150 c.c.) and methylene sulphate (12 g.) (Baker, J., 1931, 82) being added alternately in portions so that the solution did not become very strongly alkaline. After the addition was complete (1½ hours) the solution was stirred for a further ½ hour and made alkaline with potassium hydroxide, the acetone removed by distillation, and the methylenated *product* collected in ether and crystallised from light petroleum (b. p. 60—80°); it separated in prismatic needles, m. p. 102·5° (Found: C, 61·8; H, 5·[illegible] $C_{10}H_{10}O_4$ requires C, 61·8; H, 5·1%). Yield, 18%.

*4-Methoxy-2 : 3-methylenedioxyacetophenoneoxime.*—A mixture of the preceding compound (0·5 g.), hydroxylamine hydrochloride (0·165 g.; 1 mol.) and N-sodium hydroxide (2·5 c.c.) was heated on the steam-bath, and alcohol added until a clear solution was obtained, which was then refluxed for 3 hours and poured into a little water. The solid precipitate crystallised from dilute alcohol in minute prisms, m. p. 148·5° (Found: C, 57·0; H, 5·3. $C_{10}H_{11}O$[illegible] requires C, 57·3; H, 5·3%). Yield, 72%.

*4-Methoxy-2 : 3-methylenedioxyacetanilide* (III).—To the preceding oxime (0·8 g.) in [illegible]

ether (50 c.c.) was added phosphorus pentachloride (0·8 g.). After 24 hours the ether was removed by distillation, water (10 c.c.) added, and the *anilide* collected and crystallised from a small volume of hot water. It separated in bunches of needles, m. p. 138—139° (Found: N, 6·5. $C_{10}H_{11}O_4N$ requires N, 6·7%).

*4-Hydroxyveratrole*.—The preparation of this compound from 4-aminoveratrole (Fargher, J., 1920, **117**, 869) has been considerably improved and the yield raised from 20% (Robertson, J., 1932, 1385) to 45% by decomposing the diazonium salt in boiling copper sulphate solution. 4-Aminoveratrole (60 g.) in a mixture of concentrated sulphuric acid (55 c.c.) and water (500 c.c.) was diazotised at $-10°$ to $-5°$ by the addition of a solution of sodium nitrite (27 g.) in water (100 c.c.). The resulting solution was run in a thin stream into a boiling solution of copper sulphate (400 c.c.; saturated at about 30°), and, after cooling, the solution was extracted six times with ether. After the ethereal solution had been dried with sodium sulphate, the ether was distilled, and the resulting oil distilled under diminished pressure; the fraction, b. p. 160—180°/18 mm., was redistilled and yielded 4-hydroxyveratrole (27 g.) as a pale yellow oil, b. p. 173°/17 mm., m. p. about 70°. It crystallises readily from carbon tetrachloride in prisms, m. p. 80—81°; the use of a mixture of dibutyl ether and light petroleum as recommended by Clarke (*J. Amer. Chem. Soc.*, 1931, 53, 3896) is unnecessary. The *acetyl* derivative, prepared by boiling with acetic anhydride and a drop of pyridine for 10 minutes and pouring into water, separates from very dilute alcohol in hexagonal plates, m. p. 44° (Found: C, 61·4; H, 6·3. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·1%).

*5-Bromo-4-acetoxyveratrole* (IV).—4-Acetoxyveratrole (8 g.) was dissolved in acetic anhydride (20 c.c.), and a solution of bromine in acetic acid (32 c.c.; containing 20 g. of bromine in 100 c.c. of solution) added in several portions, keeping the temperature at about 10°. After a short time water was added, the solid product collected, dried (weight 6 g.), and crystallised from light petroleum (b. p. 60—80°), from which it separated in blunt-ended prisms, m. p. 67° (Found: C, 43·9; H, 4·3; Br, 29·4. $C_{10}H_{11}O_4Br$ requires C, 43·6; H, 4·0; Br, 29·1%). The same substance was also obtained by bromination of 4-hydroxyveratrole in slightly diluted acetic acid at 0° and acetylation of the product, but the yield by this method is poor. It slowly undergoes decomposition when kept in a specimen tube for several weeks. When simultaneously hydrolysed and methylated by the action of hot aqueous potassium hydroxide and methyl sulphate, it yielded 5-bromo-1 : 2 : 4-trimethoxybenzene, which separated from light petroleum (b. p. 60—80°) in rhombic prisms, m. p. 54°; the m. p. was not depressed on admixture with a specimen of 5-bromo-1 : 2 : 4-trimethoxybenzene, m. p. 54°, prepared by the direct bromination of 1 : 2 : 4-trimethoxybenzene (Fabinyi and Szeki, *Ber.*, 1910, **43**, 2679).

*5-Bromo-1 : 2 : 4-trimethoxybenzene*.—No details for the direct bromination of 1 : 2 : 4-trimethoxybenzene are given by Fabinyi and Szeki (*loc. cit.*) A solution of bromine in acetic acid (160 c.c., containing 20 g. of bromine per 100 c.c.) was added at 15° to 1 : 2 : 4-trimethoxybenzene; instant bromination occurred and the addition of a large volume of water threw down the bromo-derivative as a solid, which was crystallised from light petroleum as above (yield, 47 g.).

*2 : 3 : 5 : 2' : 3' : 5'-Hexamethoxydiphenyl*.—5-Bromo-1 : 2 : 4-trimethoxybenzene (1 g.) was added to a solution of aluminium chloride (1 g.) in either anhydrous ether (10 c.c.) or nitrobenzene (10 c.c.). After 20 hours the solvents were removed in steam, and the solid collected, boiled with dilute alkali, and recrystallised from alcohol and then acetic acid. The diphenyl derivative separated in colourless prisms, m. p. 174—175·5°, whose m. p. was not depressed on admixture with a specimen of the compound prepared by the action of copper powder on 5-bromo-1 : 2 : 4-trimethoxybenzene (Fabinyi and Szeki, *loc. cit.*). The ready formation of a diphenyl derivative is characteristic of hydroxyquinol, its trimethyl ether and derivatives (see Erdtman, *Proc. Roy. Soc.*, 1933, **143**, 198).

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## 76. *The Associating Effect of the Hydrogen Atom. Part II. Substituted Anilides and Related Substances.*

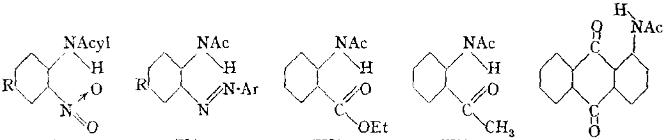
By HUBERT O. CHAPLIN and LOUIS HUNTER.

The molecular condition of 30 acylamino-compounds has been deduced from cryoscopic and wet melting-point measurements. Although certain *o*-substituted acylamines give indication of chelate ring formation between the two neighbouring

**groups, substitution of a group in the second ortho-position prevents chelation. This fact is interpreted as evidence of restricted rotation about the nitrogen-nuclear single bond in 2 : 6-disubstituted acylamines.**

THE suggestion was made in Part I (J., 1937, 1114) that the suppression of the tendency to associate in acetanilide by the substitution of certain *o*-groups may be due to chelate ring formation between such groups and the acetamido-group, involving the amide hydrogen atom. Reference to the cryoscopic measurements of von Auwers and his co-workers (*loc. cit.*) will show that the *o*-substituents most effective in this respect are hydrogen-acceptor groups such as $-NO_2$ and $-CHO$, and that other groups (*e.g.*, $CH_3$, Cl, $OCH_3$) have a relatively small effect on the association factor. It would appear, therefore, that the engagement of the amide hydrogen atom by co-ordination with a suitable *o*-substituent will prevent the intermolecular sharing of this hydrogen, which is the cause of molecular association in the amides. A similar interpretation of von Auwers's results was published by Lassettre (*Chem. Reviews*, 1937, **20**, 259) almost simultaneously with Part I of this series.

An examination has now been made of a sufficient number of substituted anilides to confirm this suggestion. In a series of nitro-acylanilines, only those derived from *o*-nitroaniline (I; R = H, Acyl = acetyl, benzoyl, *p*-toluenesulphonyl) were unassociated, the *m*- and *p*-isomers exhibiting considerable association with increasing concentration

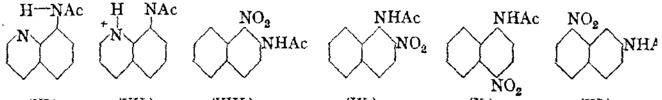


(I.) (II.) (III.) (IV.) (V.)

(Fig. 1). Similar tendencies were observed in *o*-acetamidoazo-compounds (II; Fig. 2), ethyl *o*-acetamidobenzoate (III; Fig. 3), *o*-acetamidoacetophenone (IV; Fig. 3), and 1-acetamidoanthraquinone (V).

The factors of association of these compounds were calculated from cryoscopic measurements in naphthalene, and it is significant that the *o*-compounds are almost invariably more soluble in this solvent than the *m*- and *p*-isomers. Evidence confirming a chelate structure in the *o*-compounds was also provided in the wet melting-point data. This device has been developed by Baker (J., 1934, 1687, and subsequent papers), who has interpreted the results as indicating that the isomer possessing a chelate structure shows the least depression of melting point in the presence of water. Although the limitations of this test are fully realised, the results are sufficiently parallel to those obtained cryoscopically to justify their use as confirmatory evidence.

The case of 8-acetamidoquinoline (VI) differs somewhat from those just considered in having as the hydrogen acceptor the quinoline nitrogen atom. This can accept hydrogen only by becoming an ammonium ion, and since the substance is undoubtedly chelate



(VI.) (VII.) (VIII.) (IX.) (X.) (XI.)

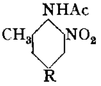
(Fig. 4), it probably exists as a resonance hybrid of (VI) and the zwitterion (VII). In this respect 8-acetamido- resembles 8-hydroxy-quinoline. As was anticipated, 6-acetamidoquinoline is associated and non-chelate (Fig. 4).

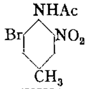
In the following comparison of four isomeric nitroacetnaphthalides it was observed th

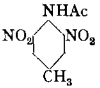
1-*nitro*-2-*acetnaphthalide* (VIII) has properties consistent with a chelate structure; it is not markedly associated, is more soluble in naphthalene, has a lower m. p., and in the

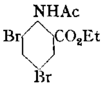
| | M. p. | Wet m. p. | Δ. | |
|---|---|---|---|---|
| 1-Nitro-2-acetnaphthalide (VIII) | 123—124° | 110° | 13—14° | Not associated. |
| 2-Nitro-1-acetnaphthalide (IX) | 199 | 166 | 33 | Associated. |
| 4-Nitro-1-acetnaphthalide (X) | 190 | 144 | 46 | Associated. |
| 8-Nitro-2-acetnaphthalide (XI) | 195 | 154 | 41 | Associated. |

presence of water shows the smallest m. p. depression of the four isomers examined. On the other hand, 2-nitro-1-acetnaphthalide (IX) has the reverse of these properties, and is much more closely comparable with the isomers (X) and (XI), in which chelation is structurally impossible. It appeared likely that the absence of a co-ordinated structure in 2-nitro-1-acetnaphthalide (IX) might be due to steric interference between the large acetyl group and the *peri*-CH group of the naphthalene nucleus, thus preventing the amide hyrogen atom from approaching sufficiently near to the nitro-group to achieve chelation. This view has been confirmed by the examination of a number of 6-substituted


(XII.)


(XIII.)


(XIV.)


(XV.)

*o*-nitroacetanilides, in which similar steric effects might be expected. The substitution of methyl (XII, R = H or $CH_3$), bromine (XIII), or nitroxyl (XIV) in the 6-position in *o*-nitroacetanilide has the same effect as the naphthalene nucleus in (IX), causing the resulting compounds to show no chelate properties, and to be associated in naphthalene solution. In a similar way the anomalous non-chelate properties of 2 : 3-dinitrophenol (Sidgwick and Aldous, J., 1921, **119**, 1008) and ethyl quinol-2 : 3-dicarboxylate (Baker and Carruthers, J., 1937, 479) are evidently due to steric interference of a type similar to that postulated above.

An interesting consequence of the chelate structure ascribed to 3-nitroaceto-*p*-toluidide (I, R = $CH_3$, Acyl = acetyl) is that it was found impossible to bring about direct bromination to 3-bromo-5-nitroaceto-*p*-toluidide (XIII). This is no doubt to be attributed to the orientation of the acetyl group, owing to chelation in (I; R = $CH_3$, Acyl = acetyl), in such a manner as to cause protection of the 3-position, thus hindering the approach of the substituting bromine. The bromination was eventually effected through the free amine, in which no such hindrance is possible, followed by acetylation.

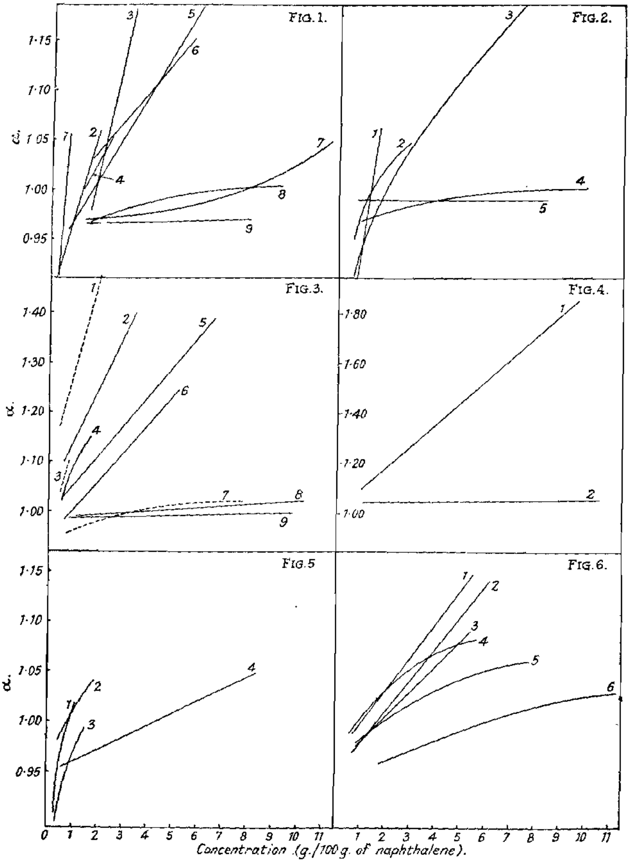
The effect of the 6-bromine atom in *ethyl* 3 : 5-*dibromo*-2-*acetamidobenzoate* (XV) is not so marked as in the case of the nitro-compounds (IX, XII, XIII, and XIV), the association–concentration curve lying midway between those typical of associated and non-associated substances (Fig. 6). This is presumably due to the stronger tendency of the carbethoxy-group, as compared with the nitro-group, to co-ordinate with hydrogen, and this conclusion is in harmony with the order of the "normalising" effect of *o*-substituents deduced by von Auwers and Pelzer (*Z. physikal. Chem.*, 1897, **23**, 449). The wet m. p. data for this substance (below), however, point to a non-chelate structure, thus

| | M. p. | Wet m. p. | Δ. |
|---|---|---|---|
| Ethyl 3 : 5-dibromo-2-acetamidobenzoate (XV) | 137° | 117° | 20° |
| Ethyl *o*-acetamidobenzoate (III) | 66 | 61 | 5 |
| *Ethyl* m-*acetamidobenzoate* | 84 | 64 | 20 |
| Ethyl *p*-acetamidobenzoate | 103—104 | 71 | 32—33 |

confirming a steric effect. It should be pointed out that the steric effect in any of the substances quoted is not assumed to prevent chelation entirely; in fact, association of such compounds is generally less marked than for typically associated compounds, and at the same time the solubility in hydrocarbon solvents is generally greater.

An inevitable consequence of the non-coplanar distribution of the acetamido-group in compounds of the 2 : 6-disubstituted acetanilide type (XII—XV) is that these substances

acquire molecular asymmetry. The failure to resolve such compounds (Tuan, Hsü, and Hsü, *J. Chinese Chem. Soc.*, 1936, **4**, 131) is probably due to rapid racemisation of the enantiomorphs; but whereas the effect of racemisation on optical rotatory power is to




diminish or destroy it, its effect on the association factor is negligible. This view been fully discussed elsewhere (*Nature*, 1937, **140**, 896).

In the following tables and curves, the association factors have been calcula according to the ideal-solution laws, and are thus to be regarded only as a semi-quantita

indication of association. Conclusions concerning association are based, not on the absolute values of the association factor (which may have no real significance), but rather on the slope of the association–concentration curves; molecular association in a substance is

FIG. 1.

1 = *p*-Nitroacetanilide.
2 = *p*-Nitrobenzanilide.
3 = *m*-Nitroacetanilide.
4 = *p'*-Toluenesulphon-*p*-nitroanilide.
5 = *m*-Nitrobenzanilide.
6 = *p'*-Toluenesulphon-*m*-nitroanilide.
7 = *o*-Nitroacetanilide (I; R = H, Acyl = COMe).
8 = *p'*-Toluenesulphon-*o*-nitroanilide (I; R = H, Acyl = $SO_2C_7H_7$).
9 = *o*-Nitrobenzanilide (I; R = H, Acyl = COPh).

FIG. 2.

1 = 1-Benzeneazo-4-acetnaphthalide.
2 = 4-Acetamido-3 : 2'-dimethylazobenzene.
3 = *p*-Acetamidoazobenzene.
4 = 1-Benzeneazo-2-acetnaphthalide.
5 = 2-Acetamido-5 : 4'-dimethylazobenzene (II; R = Me, Ar = *p*-tolyl).

FIG. 3.

1 and 5 = Ethyl-*m*-acetamidobenzoate.
2 = *m*-Acetamidoacetophenone.
3 and 6 = Ethyl *p*-acetamidobenzoate.
4 = *p*-Acetamidoacetophenone.
7 and 9 = Ethyl *o*-acetamidobenzoate (III).
8 = *o*-Acetamidoacetophenone (IV).

FIG. 4.

1 = 6-Acetamidoquinoline.
2 = 8-Acetamidoquinoline (VI).

FIG. 5.

1 = 8-Nitro-2-acetnaphthalide (XI).
2 = 4-Nitro-1-acetnaphthalide (X).
3 = 2-Nitro-1-acetnaphthalide (IX).
4 = 1-Nitro-2-acetnaphthalide (VIII).

FIG. 6.

1 = 3-Nitro-*o*-acetotoluidide (XII; R = H).
2 = 5-Nitro-4-aceto-*m*-xylidide (XII; R = Me).
3 = 3-Nitro-5-bromo-*p*-acetotoluidide (XIII).
4 = 3 : 5-Dinitro-*p*-acetotoluidide (XIV).
5 = Ethyl 3 : 5-dibromo-2-acetamidobenzoate (XV).
6 = 3-Nitro-*p*-acetotoluidide (I; R = Me, Acyl = COMe).

inferred from a steep curve, and absence of association from a flat or gently sloped curve. In the tables, concentrations are given as g./100 g. of naphthalene, *M* is the apparent molecular weight, α is the association factor, and Δ is the depression of melting point in the presence of water. Figures in parentheses indicate the normal molecular weight; those in italics are calculated from the measurements of von Auwers and Pelzer (*loc. cit.*). The broken lines in Fig. 3 are for solutions in benzene.

| | Concn. | *M*. | α. | M. p. | Wet m. p. | Δ. |
|---|---|---|---|---|---|---|
| *Acyl derivatives of the nitroanilines* (Fig. 1). | | | | | | |
| *o*-Nitroacetanilide (180) | *1·9* | *176* | *0·97* | 92° | 82° | 10° |
| (I; R = H, Acyl = $COCH_3$) | *6·8* | *179* | *0·99* | | | |
| | *11·8* | *192* | *1·07* | | | |
| *m*-Nitroacetanilide | *1·7* | *177* | *0·98* | 155 | 120 | 35 |
| | *3·2* | *213* | *1·18* | | | |
| *p*-Nitroacetanilide | *0·32* | *164* | *0·91* | 210 | 159 | 51 |
| | *0·57* | *189* | *1·05* | | | |
| | *0·76* | *190* | *1·06* | | | |
| *o*-Nitrobenzanilide (242) | 0·52 | 232·7 | 0·96 | 93 | 85 | 8 |
| (I; R = H, Acyl = COPh) | 1·48 | 234·4 | 0·97 | | | |
| | 2·93 | 232·1 | 0·96 | | | |
| | 5·10 | 234·7 | 0·97 | | | |
| | 7·92 | 234·1 | 0·97 | | | |
| *m*-Nitrobenzanilide | 0·82 | 231·3 | 0·96 | 154 | 133 | 21 |
| | 1·98 | 246·6 | 1·02 | | | |
| | 3·19 | 257·7 | 1·065 | | | |
| | 4·44 | 268·5 | 1·11 | | | |
| | 6·19 | 289·9 | 1·20 | | | |
| *p*-Nitrobenzanilide | 0·19 | 218·8 | 0·90 | 196 | 167 | 29 |
| | 0·49 | 225·6 | 0·93 | | | |
| | 1·14 | 237·8 | 0·98 | | | |
| | 1·95 * | 257·1 | 1·06 | | | |
| *p'*-Toluenesulphon-*o*-nitroanilide (292) | 1·56 | 283·0 | 0·97 | 115 | 109 | 6 |
| I; R = H, Acyl = $SO_2C_7H_7$) | 2·74 | 282·6 | 0·97 | | | |
| | 5·32 | 291·6 | 1·00 | | | |
| | 8·75 | 292·0 | 1·00 | | | |

* Solute separates at higher concentrations.

| | Concn. | *M.* | α. | M. p. | Wet m. p. | Δ. |
|---|---|---|---|---|---|---|
| *p'*-Toluenesulphon-*m*-nitroanilide | 0·72 | 293·7 | 1·01 | 138° | 117° | 21° |
| | 1·69 | 301·3 | 1·03 | | | |
| | 4·31 | 323·6 | 1·11 | | | |
| | 5·68 | 336·5 | 1·15 | | | |
| *p'*-Toluenesulphon-*p*-nitroanilide | 1·22 | 293·3 | 1·00 | 189 | 159 | 30 |
| | 2·60 * | 309·1 | 1·06 | | | |
| *p*-Acetamidoazobenzene (239) | 0·78 | 217·3 | 0·91 | 144—145 | 128 | 16—17 |
| | 2·13 | 243·3 | 1·02 | | | |
| | 3·47 | 255·7 | 1·07 | | | |
| | 4·97 | 267·8 | 1·12 | | | |
| | 7·36 | 283·2 | 1·185 | | | |
| 2-Acetamido-5 : 4'-dimethylazobenzene (267) | 0·87 | 264·3 | 0·99 | 156—157 | 142—143 | 14 |
| (II; R = Me, Ar = *p*-tolyl) | 1·96 | 262·4 | 0·98 | | | |
| | 3·55 | 265·3 | 0·99 | | | |
| | 5·76 | 264·3 | 0·99 | | | |
| | 8·43 | 264·2 | 0·99 | | | |
| 4-Acetamido-3 : 2'-dimethylazobenzene | 0·675 | 254·4 | 0·95 | 185 | 161 | 24 |
| | 1·665 | 271·6 | 1·02 | | | |
| | 2·97 * | 279·7 | 1·05 | | | |
| 1-Benzeneazo-2-acetnaphthalide (289) | 0·97 | 279·4 | 0·97 | 154 | 138 | 16 |
| | 2·48 | 282·4 | 0·98 | | | |
| | 4·69 | 284·8 | 0·99 | | | |
| | 7·05 | 288·6 | 1·00 | | | |
| | 9·93 | 289·0 | 1·00 | | | |
| 1-Benzeneazo-4-acetnaphthalide | 0·63 | 259·7 | 0·90 | 232—233 | 187—188 | 45 |
| | 1·31 | 286·6 | 0·99 | | | |
| | 1·67 * | 307·1 | 1·06 | | | |

*Acetamido-benzoates, -acetophenones, and -anthraquinones* (Fig. 3.).

| | Concn. | *M.* | α. | M. p. | Wet m. p. | Δ. |
|---|---|---|---|---|---|---|
| Ethyl *o*-acetamidobenzoate (207) (III) | 0·86 | 204·6 | 0·99 | 66 | 61 | 5 |
| | 4·46 | 204·0 | 0·99 | | | |
| | 7·43 | 201·9 | 0·975 | | | |
| | 9·69 | 204·0 | 0·985 | | | |
| (in benzene) | 0·68 | 197·4 | 0·95 | | | |
| | 2·04 | 203·2 | 0·98 | | | |
| | 3·70 | 208·0 | 1·005 | | | |
| | 5·32 | 208·9 | 1·01 | | | |
| | 7·58 | 210·6 | 1·02 | | | |
| Ethyl *m*-acetamidobenzoate | 0·71 | 213·6 | 1·03 | 84 | 64 | 20 |
| | 2·09 | 232·1 | 1·12 | | | |
| | 4·35 | 258·7 | 1·25 | | | |
| | 6·72 | 288·3 | 1·39 | | | |
| (in benzene) | 0·39 | 242·4 | 1·17 | | | |
| | 0·91 | 257·6 | 1·24 | | | |
| | 1·38 | 277·7 | 1·34 | | | |
| | 2·09 | 316·1 | 1·53 | | | |
| Ethyl *p*-acetamidobenzoate | 0·64 | 205·5 | 0·99 | 103—104 | 71 | 32— |
| | 2·04 | 220·0 | 1·06 | | | |
| | 3·71 | 243·7 | 1·18 | | | |
| | 5·22 | 257·3 | 1·24 | | | |
| (in benzene) | 0·46 | 214·5 | 1·04 | | | |
| | 0·825 * | 228·2 | 1·10 | | | |
| *o*-Acetamidoacetophenone (177) (IV) | 1·16 | 174·5 | 0·99 | 78 | 63 | 1 |
| | 3·665 | 174·4 | 0·985 | | | |
| | 6·38 | 177·2 | 1·00 | | | |
| | 10·27 | 181·6 | 1·03 | | | |
| *m*-Acetamidoacetophenone | 0·68 | 195·3 | 1·10 | 126 | 86 | 4 |
| | 1·42 | 208·3 | 1·18 | | | |
| | 2·40 | 231·8 | 1·31 | | | |
| | 3·60 | 246·7 | 1·39 | | | |
| *p*-Acetamidoacetophenone | 0·585 | 180·2 | 1·02 | 167 | 117 | |
| | 1·09 | 196·0 | 1·11 | | | |
| | 1·695 * | 203·0 | 1·15 | | | |
| 1-Acetamidoanthraquinone (265) (V) | 0·45 | 260·8 | 0·98 | 215 | 186 | |
| | 1·01 | 262·1 | 0·99 | | | |
| | 1·65 | 264·5 | 1·00 | | | |
| | 2·75 | 247·1 | 0·93 | | | |
| | 4·83 | 251·4 | 0·95 | | | |
| 2-Acetamidoanthraquinone | 0·30 * | 272·2 | 1·03 | 263 | 201 | |

* Solute separates at higher concentrations.

| | Concn. | *M.* | *a.* | M. p. | Wet m. p. | Δ. |
|---|---|---|---|---|---|---|
| *Acetamidoquinolines* (Fig. 4). | | | | | | |
| 6-Acetamidoquinoline (186) | 1·035 | 203·5 | 1·09 | 138—139° | 71° | 67—68° |
| | 2·71 | 228·1 | 1·23 | | | |
| | 6·19 | 286·1 | 1·54 | | | |
| | 9·70 | 344·6 | 1·85 | | | |
| 8-Acetamidoquinoline (VI) | 1·02 | 193·7 | 1·04 | 103 | 82 | 21 |
| | 3·63 | 193·6 | 1·04 | | | |
| | 7·73 | 192·9 | 1·04 | | | |
| | 10·61 | 196·0 | 1·05 | | | |
| *Nitroacetnaphthalides* (Fig. 5). | | | | | | |
| 1-Nitro-2-acetnaphthalide (230) (VIII) | 0·70 | 219·8 | 0·96 | 123—124 | 110 | 13—14 |
| | 1·49 | 221·5 | 0·96 | | | |
| | 2·92 | 223·6 | 0·97 | | | |
| | 4·07 | 229·5 | 1·00 | | | |
| | 5·79 | 233·6 | 1·02 | | | |
| | 8·37 | 240·5 | 1·05 | | | |
| 8-Nitro-2-acetnaphthalide (XI) | 0·355 | 209·5 | 0·91 | 195 | 154 | 41 |
| | 0·75 | 229·4 | 1·00 | | | |
| | 1·29 * | 235·3 | 1·02 | | | |
| 2-Nitro-1-acetnaphthalide (IX) | 0·31 | 206·6 | 0·90 | 199 | 166 | 33 |
| | 0·605 | 216·4 | 0·94 | | | |
| | 1·36 * | 226·9 | 0·99 | | | |
| 4-Nitro-1-acetnaphthalide (X) | 0·44 | 225·2 | 0·98 | 190 | 144 | 46 |
| | 1·21 | 234·8 | 1·02 | | | |
| | 1·86 * | 238·7 | 1·04 | | | |
| *oo'-Disubstituted derivatives of acetanilide* (Fig. 6). | | | | | | |
| 3-Nitro-*p*-acetotoluidide (194) (I; R = Me, Acyl = COMe) | 1·94 | 186 | 0·96 | 91 | 79 | 12 |
| | 5·44 | 193 | 0·995 | | | |
| | 8·88 | 198 | 1·02 | | | |
| | 11·23 | 200 | 1·03 | | | |
| 3-Nitro-*o*-acetotoluidide (XII; R = H) | 0·83 | 191·7 | 0·99 | 158 | 121 | 37 |
| | 1·29 | 195·6 | 1·01 | | | |
| | 1·71 | 198·7 | 1·02 | | | |
| | 2·41 | 202·2 | 1·04 | | | |
| | 3·34 | 206·0 | 1·06 | | | |
| | 4·17 | 212·8 | 1·10 | | | |
| | 5·525 | 222·6 | 1·15 | | | |
| 5-Nitro-4-aceto-*m*-xylidide (208) (XII; R = Me) | 0·73 | 201·8 | 0·97 | 172—173 | 144 | 28—29 |
| | 1·49 | 205·3 | 0·99 | | | |
| | 2·99 | 216·2 | 1·04 | | | |
| | 4·64 | 226·8 | 1·09 | | | |
| | 6·18 | 237·7 | 1·14 | | | |
| 3-Bromo-5-nitro-*p*-acetotoluidide (273) (XIII) | 1·025 | 267·9 | 0·98 | 210—211 | 165 | 45—46 |
| | 2·13 | 275·2 | 1·01 | | | |
| | 3·88 | 286·6 | 1·05 | | | |
| | 5·38 | 297·7 | 1·09 | | | |
| 3 : 5-Dinitro-*p*-acetotoluidide (239) (XIV) | 0·65 | 235·7 | 0·99 | 190·5 | 157 | 33·5 |
| | 1·94 | 246·7 | 1·03 | | | |
| | 3·74 | 254·3 | 1·06 | | | |
| | 5·78 | 256·9 | 1·075 | | | |
| Ethyl 3 : 5-dibromo-2-acetamido-benzoate (365) (XV) | 0·93 | 358·9 | 0·98 | 137 | 117 | 20 |
| | 2·44 | 373·9 | 1·02 | | | |
| | 5·29 | 380·6 | 1·04 | | | |
| | 7·425 | 385·7 | 1·06 | | | |

* Solute separates at higher concentrations.

## Experimental.

Molecular weights were measured cryoscopically in naphthalene; those of the ethyl acetamidobenzoates also in benzene. Wet m. p.'s were carried out in small sealed tubes of average length 1·5 cm. and average internal diameter 1·5 mm.; observations were carefully checked to eliminate the possibility of hydrolysis. Materials were prepared and purified by usual methods, and the m. p.'s of known compounds are reported only when they differ from those recorded in the literature. They are as follows: *p'*-toluenesulphon-*o*-nitroanilide, m. p. 115° (lit., 110°); *p*-acetamidoazobenzene, m. p. 144—145° (lit., 144—146°); ethyl *o*-acetamidobenzoate, m. p. 66° (lit., 61—62°, 64—65°); ethyl *p*-acetamidobenzoate, m. p. 103—104° (lit., 110°) (Found: N, 6·62. Calc.: N, 6·72%); *o*-acetamidoacetophenone, m. p. 78° (lit., 76°); ethyl 3 : 5-dibromo-*o*-aminobenzoate, m. p. 76° (lit., 74°).

The following new compounds were prepared in the course of the investigation. *Ethyl* m

*acetamidobenzoate*, prepared by acetylating the free amine, formed white needles from alcohol, m. p. 84° (Found: N, 6·64. $C_{11}H_{13}O_3N$ requires N, 6·76%). *Ethyl* 3 : *5-dibromo-o-acetamidobenzoate* was prepared by aspirating bromine vapour (2 mols.) through a solution of ethyl anthranilate (1 mol.) in glacial acetic acid, and acetylating the product (m. p. 76°) by Smith and Orton's method (J., 1908, **93**, 1249). It crystallised from aqueous alcohol in fine white needles, m. p. 137° (Found: N, 3·9. $C_{11}H_{11}O_3NBr_2$ requires N, 3·8%).

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UNIVERSITY COLLEGE, LEICESTER. [*Received, January 15th*, 1938.]

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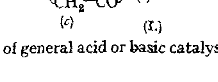
## 77. *Acid Catalysis in Non-aqueous Solvents. Part V. The Inversion of Menthone in Chlorobenzene Solution.*

By R. P. BELL and E. F. CALDIN.

The inversion of *l*-menthone in chlorobenzene at 99·4° has been studied kinetically in presence of the following acids: mono-, di-, and tri-chloroacetic, *o*-nitrobenzoic, benzoic, and picric. For the carboxylic acids there is a relation between the catalytic power in chlorobenzene and the dissociation constant in water, but the catalytic power of picric acid is much less than predicted from this relation. The degree of complex formation between menthone and mono-, di-, and tri-chloroacetic, phenylpropiolic, *m*-nitrobenzoic, benzoic, and acetic acids was investigated in chlorobenzene solution at room temperature, partly by cryoscopic measurements, and partly by observing the instantaneous change of rotation on adding the acid. There is an approximate correlation between the degree of complex formation and the dissociation constant of the acid in water, indicating that the complex formation is a protolytic reaction. The existence of this initial protolytic equilibrium is in harmony with previous views on the mechanism of prototropic reactions of this type.

PREVIOUS parts of this series (I, Bell, *Proc. Roy. Soc., A*, 1934, **143**, 377; II, Bell and Levinge, *ibid.*, 1935, **151**, 211; III, Bell and Brown, J., 1936, 1520; IV, Bell, Lidwell, and Vaughan-Jackson, *ibid.*, p. 1792) have dealt with migrations in the *N*-halogenoacylanilide series and with the depolymerisation of paraldehyde. It was desired to extend the work to prototropic reactions of the type $>CH-C=O \rightleftharpoons >C=C-OH$, which have already proved of great interest in the study of general acid–base catalysis (cf. Dawson *et al.*, J., 1926—1936; Pedersen, *J. Physical Chem.*, 1933, **37**, 751; 1934, **38**, 581, 601). In most of the kinetic work on this system the rate of prototropic change has been measured in aqueous solvents by the rate of halogenation of the substances concerned. This method is not practicable in non-dissociating solvents on account of the enormous catalytic effect of the halogen acid produced in the reaction (which in water or similar solvents is converted into the less active solvated hydrogen ion). We have therefore used the rate of change of optical activity, which in the case of the racemisation of various ketones has been shown to equal the rate of halogenation (Ingold and Wilson, J., 1934, 773; Bartlett and Stauffer, *J. Amer. Chem. Soc.*, 1935, **57**, 2580; Hsü and Wilson, J., 1936, 623).

Menthone (I) contains two centres of asymmetry, (*a*) and (*b*). Prototropic changes may occur between the carbonyl group and either of the carbon atoms (*b*) or (*c*), but of these only the former will lead to inversion. [Comparisons of the rates of inversion and of bromination (Bartlett and Vincent, *J. Amer. Chem. Soc.*, 1933, **55**, 4992) have in fact shown that 80% of the total prototropic change involves atom (*b*), though this figure is not of importance in the present work.] The kinetics of this inversion have been investigated by Tubandt (*Annalen*, 1905, **339**, 41; 1907, **354**, 259; 1910, **377**, 303), whose results deal chiefly with alcoholic solvents and basic catalysts and do not establish the presence of general acid or basic catalysis. The present work deals with catalysis by a number of acids



(I.)

in chlorobenzene solution at 99·4°: in these solutions there are no complications due to protolytic reactions between the catalyst and the solvent. Complex formation between the acids and the ketone has also been studied.

## Experimental.

*Materials.*—*l*-Menthone was prepared by the oxidation of *l*-menthol ("Organic Syntheses," Vol. I, 333) and purified by fractional distillation in a vacuum. A product of b. p. 83—84°/9—10 mm. was obtained in 65% yield. The pure liquid had $[\alpha]_D = -28{\cdot}6°$ (Beilstein gives $-28°$), and an alcoholic solution $[\alpha]_D = -25{\cdot}0°$ (Tubandt gives $-24{\cdot}8°$).

Chlorobenzene was dried over phosphoric oxide and fractionally distilled, the final product boiling within 0·2°. *p*-Chlorotoluene was redistilled twice in an all-glass apparatus and boiled within 0·1°.

Di- and tri-chloroacetic and *m*-nitro- and *m*-chloro-benzoic acids were pure commercial specimens. *o*-Nitrobenzoic acid was recrystallised from aqueous alcohol, benzoic acid from toluene, and monochloroacetic acid twice from benzene. Phenylpropiolic acid was prepared from cinnamic acid ("Organic Syntheses," Vol. XII, 37, 60) and recrystallised from water. All materials and solutions were kept in desiccators.

*Measurement of Reaction Velocity.*—The rotation was measured with a Schmidt and Haensch polarimeter, a sodium lamp being used as a source of light. Each reading was the mean of 4—6 settings, and was accurate to about 0·01°. The value of $[\alpha]_D$ for solutions of *l*-menthone in chlorobenzene was found to be independent of concentration. It was also shown by Tubandt (*loc. cit.*) that the rotations of *l*-menthone and *d*-*iso*menthone are additive.

The table of the polarimeter was removed to accommodate a small metal thermostat containing medicinal paraffin, controlled to 99·4° ± 0·05°. Two polarimeter tubes (100 mm. with adhesed ends) were cemented into short copper tubes soldered into the front and back of the thermostat. Considerable difficulty was experienced in finding a cement which would adhere to glass and copper and also be unaffected by paraffin at 100° over long periods. The proprietary cement "Semmentum" (left to harden for a few hours and then baked at 110°) was eventually found to be satisfactory. The same cement was used to attach a vertical glass tube to the filling aperture of the polarimeter tube, which could be closed below thermostat level by a ground-in glass plug. The whole thermostat could be moved laterally by a rack-and-pinion device in order to bring one or other of the two tubes into the field of view of the polarimeter.

Tests with a thermocouple showed that the temperature did not vary by more than 0·1° from one part of the polarimeter tube to another, and it was found that a solution acquired thermostat temperature to within 0·1° about 10 minutes after being introduced into the polarimeter tube. Some of the slowest experiments were carried out in the vessels previously described by Bell and Levinge (*loc. cit.*), which were periodically removed from the thermostat and cooled, polarimeter measurements being made at room temperature. By observing the rates of heating and cooling, it was possible to allow approximately for the amount of reaction occurring during this period: the time correction amounted only to about one minute for each reading.

In each reaction 20—40 readings were taken, and the first-order velocity constant calculated by Guggenheim's method (*Phil. Mag.*, 1926, **2**, 538). The first set of readings normally covered 60—90% of the reaction, and no significant deviations from a unimolecular course were observed. Table I gives the individual readings for a typical reaction, the calculated values of $\Delta r$ being given by $\log_{10} \Delta r = 0{\cdot}412 - 0{\cdot}00311t$.

*Kinetic results.* Stability tests showed that, in the absence of acid, chlorobenzene solutions of menthone exhibit no change in rotation over the longest period employed in the catalytic experiments. The results obtained in acid solutions are given in Tables II and III. Table II

Table I.

0·0201N-Trichloroacetic acid; 0·90% menthone.

| Time (mins.). | $\Delta r$ Calc. | $\Delta r$ Obs. | Diff. | Time (mins.). | $\Delta r$ Calc. | $\Delta r$ Obs. | Diff. | Time (mins.). | $\Delta r$ Calc. | $\Delta r$ Obs. | Diff. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | 2·24° | 2·22° | +0·02° | 95 | 1·31° | 1·33° | −0·02° | 169 | 0·77° | 0·77° | ±0·00° |
| 32 | 2·06 | 2·02 | +0·04 | 108 | 1·19 | 1·23 | −0·04 | 180 | 0·71 | 0·72 | −0·01 |
| 46 | 1·86 | 1·87 | −0·01 | 120 | 1·10 | 1·09 | +0·01 | 182 | 0·70 | 0·69 | +0·01 |
| 60 | 1·68 | 1·70 | −0·02 | 130 | 1·02 | 1·05 | −0·03 | 190 | 0·66 | 0·67 | −0·01 |
| 75 | 1·51 | 1·51 | ±0·00 | 142 | 0·94 | 0·94 | ±0·00 | 202 | 0·61 | 0·59 | +0·02 |
| 87 | 1·39 | 1·41 | −0·02 | 156 | 0·85 | 0·83 | +0·02 | | | | |

contains results for various menthone concentrations, while for results in Table III the menthone concentration was kept constant at 6·2 ± 0·2%. The symbols used are: $x$ = menthone concentration, weight %; $c$ = acid concentration, moles per 1000 g. of solution; $k$ = first-order velocity constant, mins.$^{-1}$, $\log_{10}$.

TABLE II.

*Dichloroacetic acid.*

| $c$. | $x$. | $10^4k$ (obs.). | $10^4k$ (calc.). |
|---|---|---|---|
| 0·053 | 0·0 | (31·5) | — |
| | 3·48 | 27·9 | 25·2 |
| | 6·25 | 20·4 | 20·1 |
| | 8·77 | 13·7 | 15·7 |
| 0·069 | 0·0 | (44·6) | — |
| | 4·36 | 38·4 | 33·4 |
| | 6·00 | 26·4 | 29·5 |
| | 7·71 | 24·9 | 25·0 |
| | 9·57 | 19·3 | 20·1 |
| 0·107 | 0·0 | (94·5) | — |
| | 3·41 | 81·8 | 76·3 |
| | 6·30 | 65·7 | 60·7 |
| | 8·80 | 39·8 | 47·5 |
| 0·138 | 0·0 | (140) | — |
| | 3·49 | 117 | 112 |
| | 4·91 | 99·5 | 101 |
| | 6·40 | 96·0 | 88·5 |
| | 7·40 | 76·0 | 81·2 |
| | 8·75 | 66·7 | 70·0 |

*Trichloroacetic acid.*

| $c$. | $x$. | $10^4k$ (obs.). | $10^4k$ (calc.). |
|---|---|---|---|
| 0·020 | 0·0 | (49·3) | — |
| | 4·52 | 33·9 | 36·6 |
| | 5·40 | 37·5 | 34·1 |
| | 6·15 | 27·0 | 32·1 |
| | 6·90 | 31·6 | 30·2 |
| | 7·80 | 29·6 | 27·7 |
| 0·029 | 0·0 | (84·8) | — |
| | 4·68 | 56·9 | 61·8 |
| | 6·24 | 49·9 | 54·2 |
| | 7·35 | 54·9 | 49·2 |
| | 8·75 | 44·5 | 42·4 |
| 0·051 | 0·0 | (180) | — |
| | 4·61 | 128 | 134 |
| | 6·15 | 116 | 117 |
| | 7·92 | 104 | 99·2 |

TABLE III.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *Benzoic acid.* | | | | | | | |
| $c$ ........................... | 0·068 | 0·199 | 0·304 | 0·400 | 0·654 | | |
| $10^4k$ (obs.) ............... | 1·11 | 2·43 | 3·02 | 4·36 | 5·38 | | |
| $10^4k$ (calc.) ............... | 1·15 | 2·35 | 3·16 | 3·85 | 5·44 | | |
| m-*Chlorobenzoic acid.* | | | | | | | |
| $c$ ........................... | 0·111 | 0·156 | 0·218 | 0·258 | 0·288 | 0·391 | |
| $10^4k$ (obs.) ............... | 3·20 | 3·90 | 4·82 | 5·80 | 6·02 | 7·30 | |
| $10^4k$ (calc.) ............... | 3·17 | 3·93 | 4·90 | 5·50 | 5·95 | 7·38 | |
| *Monochloroacetic acid.* | | | | | | | |
| $c$ ........................... | 0·110 | 0·163 | 0·214 | 0·252 | 0·276 | 0·336 | 0·371 |
| $10^4k$ (obs.) ............... | 5·3 | 8·3 | 13·0 | 14·8 | 24·3 | 22·9 | 33·2 |
| $10^4k$ (calc.) ............... | 4·8 | 8·2 | 12·3 | 15·9 | 18·4 | 25·1 | 29·5 |
| o-*Nitrobenzoic acid.* | | | | | | | |
| $c$ ........................... | 0·112 | 0·172 | 0·207 | 0·256 | 0·275 | 0·297 | |
| $10^4k$ (obs.) ............... | 12·1 | 21·4 | 27·5 | 28·1 | 34·1 | 41·7 | |
| $10^4k$ (calc.) ............... | 11·5 | 19·7 | 25·2 | 33·6 | 37·1 | 41·4 | |
| *Dichloroacetic acid.* | | | | | | | |
| $c$ ........................... | 0·0097 | 0·0212 | 0·0295 | 0·0395 | 0·0526 | 0·0594 | 0·068 |
| $10^4k$ (obs.) ............... | 1·8 | 8·2 | 9·6 | 19·2 | 19·9 | 24·0 | 25·0 |
| $10^4k$ (calc.) ............... | 2·2 | 5·8 | 9·6 | 13·4 | 20·2 | 24·3 | 29·8 |
| $c$ ........................... | 0·078 | 0·103 | 0·138 | | | | |
| $10^4k$ (obs.) ............... | 35·5 | 61·4 | 93·8 | | | | |
| $10^4k$ (calc.) ............... | 37·0 | 58·0 | 89·8 | | | | |
| *Trichloroacetic acid.* | | | | | | | |
| $c$ ........................... | 0·0104 | 0·0194 | 0·0288 | 0·0384 | 0·0485 | 0·0505 | |
| $10^4k$ (obs.) ............... | 11·4 | 25·8 | 56·7 | 89·0 | 106·5 | 90·0 | |
| $10^4k$ (calc.) ............... | 11·3 | 27·1 | 49·3 | 78·1 | 114 | 122 | |
| *Picric acid.* | | | | | | | |
| $c$ ........................... | 0·099 | 0·149 | 0·194 | 0·245 | | | |
| $10^4k$ (obs.) ............... | 10·5 | 20·5 | 28·0 | 49·0 | | | |
| $10^4k$ (calc.) ............... | 10·4 | 20·1 | 31·6 | 48·0 | | | |

*Effect of Menthone Concentration.*—The results in Table II show a linear variation velocity constant with menthone concentration. Moreover, all the results can expressed approximately by

$$k = k_0(1 - \gamma x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad ($$

where $\gamma$ is independent of the acid concentration and is given the same value for catalysis by trichloro- and dichloro-acetic acids. The last column of Table II contains the values of $k$ calculated from equation (1) with $\gamma = 0{\cdot}057$ throughout. The extrapolated values of $k_0$ are shown in parentheses.

*Effect of Acid Concentration.*—Since the menthone was found to exert a constant "medium effect" in catalysis by both tri- and di-chloroacetic acids at different concentrations, the remainder of the catalytic experiments were carried out at a constant menthone concentration of about 6%, giving a total change in rotation of about 2°. The velocity constants thus obtained should be comparable, and can be used to determine the effect of the nature and concentration of the catalyst.

It is clear from Table II that the velocity is not in general proportional to the acid concentration, varying sometimes more and sometimes less rapidly than a linear relation demands. This behaviour has not been fully accounted for, but for the purpose of comparing the catalytic power of different acids we have expressed the results by one of the two following equations :

$$k = k_A c + a\sqrt{c} \quad \ldots \quad (2)$$
$$k = k_A c + bc^2 \quad \ldots \quad (3)$$

where $k_A$, $a$, and $b$ are all positive constants. The best values of these constants were determined graphically and are given in Table IV, together with the dissociation constants of the acids.

TABLE IV.

| Acid. | $10^4 a$. | $10^4 k_A$. | $b$. | $K_A$. 25°. | $K_A$. 100°. |
|---|---|---|---|---|---|
| Benzoic | 3·3 | 4·4 | — | $6{\cdot}6 \times 10^{-5}$ | $4{\cdot}5 \times 10^{-5}$ |
| *m*-Chlorobenzoic | 6·8 | 8·0 | — | $1{\cdot}6 \times 10^{-4}$ | — |
| Monochloroacetic | — | 28 | 0·014 | $1{\cdot}6 \times 10^{-3}$ | $4{\cdot}7 \times 10^{-4}$ |
| *o*-Nitrobenzoic | — | 80 | 0·020 | $6{\cdot}3 \times 10^{-3}$ | $1{\cdot}6 \times 10^{-3}$ |
| Dichloroacetic | — | 200 | 0·35 | $5{\cdot}5 \times 10^{-2}$ | $(5 \times 10^{-2})$ |
| Trichloroacetic | — | 740 | 3·4 | $8 \times 10^{-1}$ | — |
| Picric | — | 58 | 0·062 | — | — |

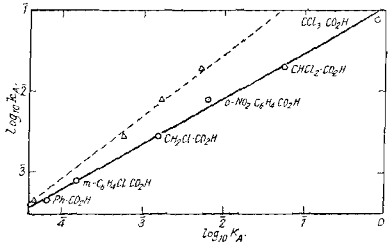
The values of $k$ calculated from these equations are given in Table III. There are no systematic discrepancies, though in a few cases the deviations are considerably greater than the expected experimental error.

Equations (2) and (3) must be regarded as largely empirical, though it is possible to obtain some sort of justification for the non-linear terms. For instance, carboxylic acids are known to exist largely as double molecules in hydrocarbon solvents, and if the prototropic change involves the interaction of menthone with a single acid molecule, a term proportional to $\sqrt{c}$ will result. Similarly, the term in $c^2$ may be interpreted as a linear medium effect. It is probable that the complete theoretical expression for the variation of $k$ with $c$ would involve at least three terms, especially in view of the results on complex formation described below. However, the kinetic data are not sufficiently accurate or extensive to warrant the use of a more complicated expression, and it should be emphasised that the value of the coefficient $k_A$ in the linear term will not be much affected by the form adopted for the rest of the equation. We may therefore use the $k_A$ coefficients for comparing the catalytic power of different acids.

*The Relation between Catalytic Power and Acid Strength.*—Recent work on protolytic equilibria in aprotic solvents (cf. Bell, *Ann. Reports*, 1934, **31**, 79) indicates that the dissociation constants in water can be used as an approximate measure of the relative strengths of acids in these solvents. [There is in any case some justification for using the values in water as a measure of the "intrinsic" strength : cf. Wynne-Jones, *Proc. Roy. Soc.*, **1933**, *A*, **140**, **440** : Bell, *Ann. Reports*, 1934, **31**, 78.] These dissociation constants (at 25°) are given in col. 5 of Table IV. For all the carboxylic acids studied there is clearly a correlation between the catalytic constant $k_A$ and the dissociation constant $K_A$, and the plot of $\log_{10} k_A$ against $\log_{10} K_A$ (Fig. 1; circles) shows that this relation is a quantitative one of the type first proposed by Brönsted and Pedersen (*Z. physikal. Chem.*, 1924, **108**, 185). The slope of the heavy straight line in Fig. I is 0·6.

[It would be more satisfactory to use dissociation constants relating to the temperature of the kinetic experiments (*ca.* 100°) in place of those at 25°. Actual measurements at or near 100° are available only for benzoic and *o*-nitrobenzoic acids (cf. Landolt–Börnstein's "Tabellen"), but for monochloroacetic acid there are accurate measurements in the range 0—40° (Wright, *J. Amer. Chem. Soc.*, 1934, **56**, 314) which can be extrapolated to 100° with some confidence by means of the empirical relation proposed by Harned and Embree (*ibid.*, p. 1050). For dichloroacetic acid a tentative value at 100° can be derived by extrapolating the values given up to 45° by Bell and Baughan (*Proc. Roy. Soc.*, 1937, *A*, **158**, 464) on the basis of catalysis by the dichloroacetate ion. These four values are given in the last column of Table IV and are plotted as triangles in Fig. 1. It appears that the use of dis-

FIG. 1.




sociation constants at 100° would increase the exponent of the Brönsted relation, the broken line in the figure having a slope of 0·75.]

Picric acid has a very much smaller catalytic effect than would be expected from its strength in water. The same behaviour has been observed in other catalysed reactions in non-aqueous solvents (Brönsted and Bell, *J. Amer. Chem. Soc.*, 1931, **53**, 2478; Bell, *Proc. Roy. Soc.*, 1934, *A*, **143**, 377; where the causes of this anomaly are discussed).

*The Reaction Mechanism.*—The mechanism of the prototropic change may be represented by the scheme

$$>CH\cdot CO- + HA \underset{k_2}{\overset{k_1}{\rightleftarrows}} \left\{\begin{array}{l}>CH\cdot C(OH^+)- \\ >CH^+\cdot C(OH)-\end{array}\right\} + A^- \quad . \quad . \quad . \quad . \quad (4)$$
$$\xrightarrow{k_3} >C{:}C(OH)- + HA$$

where the ion represented in brackets is a single species having a configuration intermediate between the two formulæ given: $k_1$, $k_2$, and $k_3$ are the bimolecular velocity constants for the processes concerned. For a reaction taking place in aqueous solution, the base which removes a proton from the ion is most likely to be a water molecule, but in an aprotic solvent like chlorobenzene the only base available is the anion of the catalyst acid; moreover, owing to the low dielectric constant of the medium this anion will not exist in a free state but will be associated with the cation formed from the ketone. Lowry's view that prototropic change demands the simultaneous presence of an acid and a base thus requires a special interpretation in the present case, since the addition of an acid alone serves to effect both the addition and the removal of a proton.

The removal of a proton from the cation may take place from either the oxygen or the carbon atom, and it is only in the latter case that racemisation will take place. If $k_2 \ll k_3$ the rate of racemisation will be determined by the rate of formation of the cation, and we are dealing with a true general acid catalysis. If, on the other hand, $k_2 \gg k_3$ the cation will be in equilibrium with the ketone and the rate is determined by the rate at which it loses a proton from the carbon atom; *i.e.*, we are actually measuring general basic catalysis of the cation. These possibilities have been considered by various authors (Pedersen, *J. Physical*

*Chem.*, 1934, **38**, 581; *Trans. Faraday Soc.*, 1938, **34**, 237; Bonhoeffer and Reitz, *Z. physikal Chem.*, 1937, *A*, **179**, 135), who conclude that the latter case is the one applicable to prototropy in ketones, since the electronic structure of the cation will be nearly the same as that of the keto-form (cf. also Nathan and Watson, J., 1933, 217). The observed acid catalytic constant $k_A$ can thus be written in the form

$$k_A = k_1k_3/k_2 = Kk_3 \qquad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where $K$ is the equilibrium constant for the protolytic equilibrium between acid and ketone, and $k_3$ a catalytic constant for reaction of the ketone cation with the basic anion $A^-$. If $K_A$ is the dissociation constant of the acid in water, then for a series of similar acids we should expect the following relations to hold approximately

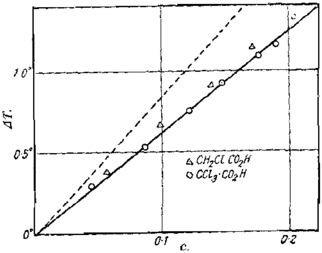
$$K \propto K_A;\ k_3 \propto (1/K)^\alpha\ (\alpha < 1) \qquad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

leading to the observed relation between catalytic power and acid strength

$$k_A \propto K_A{}^{1-\alpha} \qquad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

*Study of Complex Formation.*—It has also been found possible to observe directly the initial protolytic equilibrium between the ketone and the acid. It is usually assumed that in reactions of this kind the amounts of the intermediate cation present are very small, and this is probably the case in aqueous solution; however, in the present case there were indications of appreciable interaction with strong acids even at 99·4°, since if the rotations of menthone solutions containing tri- or di-chloroacetic acid were extrapolated back to zero time, the values obtained were always smaller than the value for pure menthone in chlorobenzene. This extrapolation was, however, inaccurate, and investigations were therefore carried out at lower temperatures, where the inversion is very slow and the reaction between ketone and acid will take place to a greater extent.

FIG. 2.




In a solvent of low dielectric constant the cation and anion shown in equation (4) will not exist independently, but will be present as an ion-pair. It should therefore be possible to detect this complex formation by cryoscopic measurements. Chlorobenzene itself melts at − 45°, and measurements were therefore made in the very similar solvent *p*-chlorotoluene (m. p. 6·86°), using the method previously described (Bell, Baughan, and Vaughan-Jackson, J., 1934, 1969). The results obtained are given in Table V.

TABLE V.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *Trichloroacetic acid + menthone; equimolecular proportions.* | | | | | | | |
| $c$ | 0·044 | 0·086 | 0·121 | 0·147 | 0·176 | 0·190 | |
| $\Delta T$ | 0·29° | 0·53° | 0·75° | 0·92° | 1·09° | 1·15° | |
| *Monochloroacetic acid + menthone; equimolecular proportions.* | | | | | | | |
| $c$ | 0·056 | 0·098 | 0·138 | 0·171 | 0·204 | | |
| $\Delta T$ | 0·37° | 0·66° | 0·91° | 1·14° | 1·33° | | |
| *Trichloroacetic acid + menthone; proportions* M + 2A. | | | | | | | |
| $c$ | 0·090 | 0·128 | 0·156 | 0·181 | 0·218 | 0·242 | 0·274 |
| $\Delta T$ | 0·33° | 0·45° | 0·56° | 0·64° | 0·76° | 0·86° | 0·98° |
| $\Delta T$ (calc.) (*a*) | 0·27 | 0·38 | 0·46 | 0·54 | 0·65 | 0·72 | 0·81 |
| $\Delta T$ (calc.) (*b*) | 0·41 | 0·58 | 0·70 | 0·81 | 0·98 | 1·09 | 1·24 |

The freezing-point depressions for mixtures of menthone with equivalent quantities of tri- and mono-chloroacetic acids are plotted in Fig. 2, and the full and the broken line

represent the theoretical relations for complete and zero association respectively. It is clear that complex formation is complete with trichloroacetic and less complete with monochloroacetic acid. However, the carboxylic acids are present almost exclusively as double molecules at the concentrations studied (cf. Bell, Baughan, and Vaughan-Jackson, *loc. cit.*), so these results do not distinguish between the two types of association :

$$\left.\begin{array}{l}(a)\ 2M + (HA)_2 \longrightarrow M + M(HA)_2 \\ (b)\ 2M + (HA)_2 \longrightarrow 2M(HA)\end{array}\right\} 3 \text{ mols.} \longrightarrow 2 \text{ mols.} \quad . \quad . \quad (8)$$

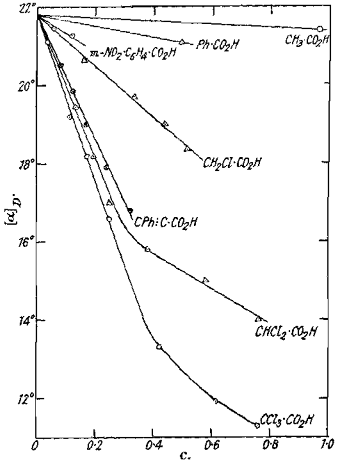
It was hoped to decide this point for trichloroacetic acid by experiments with 2 mols. of this acid per mol. of menthone, the two types of association giving

$$(a)\ M + (HA)_2 \longrightarrow M(HA)_2\ (2 \text{ mols.} \longrightarrow 1 \text{ mol.})$$

$$(b)\ 2M + 2(HA)_2 \longrightarrow 2M(HA) + (HA)_2\ (4 \text{ mols.} \longrightarrow 3 \text{ mols.})$$

The results are given in the last section of Table V, together with the freezing-point depressions calculated on the two assumptions (*a*) and (*b*). The experimental results are always

FIG. 3.




intermediate between the two theoretical possibilities. This may indicate that both typ of complex are formed; on the other hand, it must be remembered that if the complex consist of ion-pairs they will deviate considerably from simple thermodynamic behavio in a medium of low dielectric constant (cf. Fuoss, *J. Amer. Chem. Soc.*, 1934, **56**, 1027 thus making it difficult to interpret the cryoscopic data quantitatively.

For comparing the degree of complex formation with a series of acids, we have used t depression of the optical rotation; this is experimentally more convenient and accura than cryoscopy, and will be less affected by thermodynamic abnormalities. This depressi is instantaneous, confirming the view advanced in the last section that the initial trans of a proton from the acid to the menthone does not determine the rate of inversion. Ta VI contains the results obtained in chlorobenzene solution at room temperature, and th are shown graphically in Fig. 3.

TABLE VI.

(Menthone concentration = $6 \cdot 1 \pm 0 \cdot 2\%$ throughout.)

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *Trichloroacetic acid.* | | | | | | | |
| $c$ | 0·036 | 0·112 | 0·171 | 0·252 | 0·420 | 0·616 | 0·762 |
| $[\alpha]_D$ | 21·1° | 19·2° | 18·2° | 16·6° | 13·3° | 11·0° | 11·3° |
| *Dichloroacetic acid.* | | | | | | | |
| $c$ | 0·133 | 0·194 | 0·256 | 0·383 | 0·590 | 0·760 | |
| $[\alpha]_D$ | $19 \cdot 4_5$° | 18·2° | 16·8° | 15·8° | 15·0° | 14·0° | |
| *Phenylpropiolic acid.* | | | | | | | |
| $c$ | 0·080 | 0·120 | 0·168 | 0·237 | 0·322 | | |
| $[\alpha]_D$ | 20·5° | $19 \cdot 8_5$° | 19·0° | 17·9° | 16·8° | | |
| *Monochloroacetic acid.* | | | | | | | |
| $c$ | 0·158 | 0·332 | 0·438 | 0·514 | | | |
| $[\alpha]_D$ | $20 \cdot 6_5$° | 19·7° | 19·0° | 18·35° | | | |
| m-*Nitrobenzoic acid.* | | | | | | | |
| $c$ | 0·056 | 0·118 | | | | | |
| $[\alpha]_D$ | $21 \cdot 4_5$° | 21·3° | | | | | |

| | | | |
|---|---|---|---|
| *Benzoic acid.* | | *Acetic acid.* | |
| $c$ | 0·492 | $c$ | 0·965 |
| $[\alpha]_D$ | 21·1° | $[\alpha]_D$ | 21·4° |

It will be seen that the depressions in $[\alpha]_D$ increase in the same order as the dissociation constants of the acids: this will also be true of the degree of complex formation provided that the rotation of the complex formed be roughly independent of the nature of the acid. This fact agrees with the supposition that complex formation is due to a protolytic equilibrium. As might be expected from the cryoscopic results, both the equilibrium constants calculated on the basis of equation (8) were found to vary considerably with concentration.

The somewhat complicated state of affairs found in these experiments may account partly for the absence of any simple relation between the rate of inversion and the acid concentration, though the degree of complex formation will be considerably smaller at 100° than at room temperature.

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## 78. *Researches in the Phenanthridine Series. Part V. The Colour and Antiseptic Properties of Quaternary Salts.*

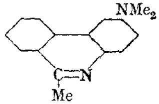
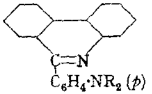
By SIR GILBERT MORGAN and LESLIE P. WALLS, with a Note by C. H. BROWNING, R. GULBRANSEN, and J. V. M. ROBB.

In Parts I and II the preparation was described of various phenanthridine compounds containing amino-groups, and of quaternary salts derived from them analogous to those of the acridine series. This work has now been amplified, particularly with a view to gaining information on the colour and antiseptic properties of phenanthridinium compounds.

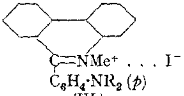
By methylation of the corresponding compounds containing primary amino-groups the ditertiary amines, 3-dimethylamino-9-methyl- and 9-*p*-dimethylamino-phenyl-phenanthridine have been prepared, and from the latter the three possible quaternary salts have been obtained. The colours of the latter conform to a theory of benzenoid-quinonoid resonance. Further information on the mechanism of the conversion of acyl-*o*-xenylamines into phenanthridine compounds has led to the synthesis of two series based on 3(and 7)-amino-9-*p*-aminophenylphenanthridine, and certain quaternary salts derived from these triamines have unexpected trypanocidal properties. In addition, the antiseptic properties of thirty-one compounds, including a series of amino-compounds derived from 9-chloro- and 9-ω-chloromethyl-phenanthridine, are reported on by Professor C. H. Browning and his collaborators, and some are shown to be powerfully active both in peptone water and in a serum medium.

In Parts I and II (J., 1931, 2451; 1932, 2230) attention was drawn to the colour of certain quaternary salts of the series, which also contained primary amino-groups. Further information has been obtained by replacement of the latter by tertiary amino-groups, and by the study of other series of salts. At the same time a comprehensive series of salts has become available for the investigation of antiseptic properties. In addition, a number of derivatives of 9-chloro- and 9-ω-chloromethyl-phenanthridine have been prepared for the latter purpose.

3-Amino-9-methylphenanthridine (J., 1932, 2228) was smoothly converted by methyl iodide into the dimethylamino-compound (I), but pure quaternary salts could not be obtained therefrom by further methylation.

(I.)   (II.)

9-*p*-Aminophenylphenanthridine (II; R = H) (J., 1931, 2454) was similarly converted into a tertiary amine (II; R = Me), and from the latter all three possible quaternary salts were obtained: the red *hetero-N*-salt (III; R = Me), the white *ar-N*-salt (IV), and the diquaternary salt (V). Although the di-iodide (V) is yellow, the corresponding dichloride is white, the yellow colour being due possibly to a like cause to that of mercuric iodide. These constitutions were confirmed by methylation of 9-*p*-aminophenyl-10-methylphenanthridinium iodide (III; R = H), whereby (III; R = Me) and (V) alone were obtained.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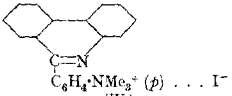
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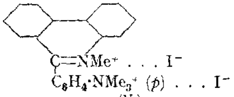
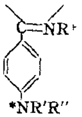
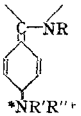

(V.)

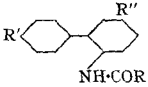
The colour relationships of the series derived from (II) may now be summarised. Bases, primary and tertiary, and acetyl derivatives are colourless or almost so, but monoacid salts and those with *hetero-N* alone quaternary are red. The appearance of colour is always associated with the possibility of valency tautomerism (involving electron displacements only), and thus is probably due to a like cause to that of the basic dyes of the acridine, cyanine and triphenylmethane series, namely, wave-mechanical resonance; the true structure of a coloured salt is intermediate between the benzenoid (VI) and the quinonoid (VII) forms (R = H or Me).

(VI.)   (VII.)

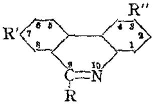
When *ar-N** is quaternary, this valency tautomerism is impossible; when R′ = H and R″ = CO·$CH_3$, it is largely suppressed. It follows that in the coloured monoacid salt, proton attaches itself to *hetero-N*.

In the synthesis of phenanthridine derivatives (IX) from acyl-*o*-xenylamines (VIII) with the agency of phosphorus oxychloride considerable resinification may occur, which is due probably to a side reaction involving elimination of the acyl group. The side reaction predominates when in (VIII) R = Me, R′ = $NO_2$, and R″ = H (or $NO_2$). When acetyl is replaced by a less readily removable group (R = $C_6H_5$ or *p*-$C_6H_4$·$NO_2$), the side reaction is suppressed and ring closure occurs, though very slowly. Appreciation of this factor has

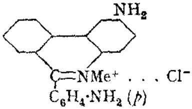
led to two series of derivatives, from which isomerides of chrysaniline have been prepared. 5-Nitro-2-*p*-nitrobenzamidodiphenyl (VIII; R = *p*-$C_6H_4{\cdot}NO_2$, R′ = H, R″ = $NO_2$) was converted into 3-nitro-9-*p*-nitrophenylphenanthridine (IX; R = *p*-$C_6H_4{\cdot}NO_2$, R′ = H, R″ = $NO_2$), which was readily reduced to the diamino-compound. Addition of methyl *p*-toluenesulphonate to the diacetyl derivative of the diamine converted it into a quaternary



(VIII.)

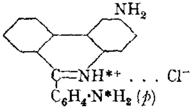


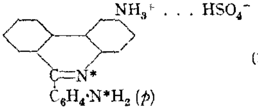
(IX.)



(X.)

(XI.)



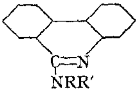


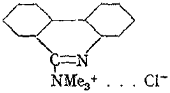
(XII.)

salt, which, after hydrolysis of the acetyl groups, yielded red 3-amino-9-*p*-aminophenyl-10-methylphenanthridinium chloride (X). The series corresponding to 7-amino-9-*p*-aminophenylphenanthridine was similarly prepared.

The colour relationships of these chrysaniline analogues conform to the foregoing postulates, except that, whereas the hydrobromide of 3-amino-9-*p*-aminophenylphenanthridine is red, the sparingly soluble sulphate is almost colourless. In a salt of this type, proton can attach itself to one of three possible basic centres: if it chooses the *hetero-N* (XI), the salt should be coloured, but if the attachment is to either primary amino-group (compare XII), the salt would probably be colourless. The sulphate may be of the latter type, but the hydrobromide of the former. The second stage of ionisation of sulphuric acid may be effective, however, so that in the colourless salt as in (V) two basic centres (indicated by * in XI and XII) are satisfied with consequent suppression of valency tautomerism. This alternative explanation is not supported by the fact that the sulphate of 7-amino-9-*p*-aminophenylphenanthridine, for which similar arguments should apply, is coloured.

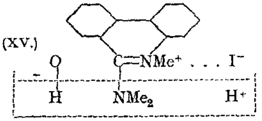
(XIII.)

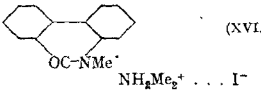




(XIV.)

(XV.)





(XVI.)

9-Chlorophenanthridine condensed with mono-, di- and tri-methylamine to yield respectively 9-methyl- (XIII; R = H, R′ = Me), 9-dimethyl- (XIII; R = R′ = Me) aminophenanthridine, and 9-phenanthridyltrimethylammonium chloride (XIV). The diamine (XIII; R = R′ = Me) was further methylated to 9-dimethylamino-10-methylphenanthridinium iodide (XV), which was unexpectedly unstable in hot aqueous solution; it was converted smoothly into *N*-methylphenanthridone (XVI), a hydrolysis which establishes its constitution.

9-ω-Chloromethylphenanthridine likewise condensed readily with trimethylamine, piperidine and pyridine with the formation of similar compounds.

*Note on the Antiseptic Action of Certain Phenanthridine Compounds.*†

The method of measuring antiseptic activity is that previously used by the authors (Browning and Gulbransen, *Brit. J. Exp. Path.*, 1921, **2**, 95; Browning, Cohen, Gaunt, and Gulbransen, *Proc. Roy. Soc.*, 1922, *B*, **93**, 329; Browning, Cohen, Ellingworth, and Gulbransen, *ibid.*, 1926, *B*, **100**, 293). Two media were employed: (a) a 0·7% solution of bacteriological peptone in 0·35% sodium chloride solution adjusted to a $p_H$ of 7·2—7·8 and (b) sterile ox serum previously heated for several hours at 56° (only such specimens of serum were used as yielded good growths of *B. coli*). Each medium in 1 c.c. amounts, containing various concentrations of the substances to be tested, was inoculated with 0·1 c.c. of a 1 : 1000 dilution of a 24 hours' culture of *Staphylococcus aureus* or *B. coli*. The results were read after 48 hours at 37°, inhibition of growth being judged by absence of obvious turbidity of the originally clear medium and by sterility or very limited growth when a loopful of the mixture was subcultured on agar. The lowest concentration of each substance which produced this result, termed the "inhibitory concentration," has been ascertained. This value yields the most satisfactory indication of the antiseptic power of slowly acting bactericidal agents such as complex organic compounds usually are. It is employed in preference to the sterilising concentration for purposes of comparison of compounds, because inhibition of bacterial growth may be produced over a wide range of concentrations before the actual sterilising concentration is attained. Also in repeated tests the concentration of antiseptic at which inhibition first occurs tends to be more constant than that at which complete sterilisation is effected.

Thirty-one phenanthridine compounds were examined for antiseptic properties; appropriate references are given, numbers otherwise referring to the experimental section. Phenanthridine hydrochloride (1*;‡ Pictet and Ankersmit, *Ber.*, 1889, **22**, 3340) has only a moderate antiseptic action in aqueous medium, and this is diminished in serum. The activity of the molecule is not significantly increased by the simultaneous introduction of a methyl group into the 9-position and an amino-group (2) or dimethylamino-group (3) into the 3-position. Similarly, the presence of an amino-group attached to the 9-C atom as in 9-aminophenanthridine (24; J., 1932, 2230), or of a methylamino-group (25), or dimethylamino-group (26) does not markedly affect the antiseptic action. 9-Phenanthridyltrimethylammonium iodide (27) is also of the same order of potency as phenanthridine.

9-ω-Phenanthridylmethyltrimethylammonium iodide (29*) is similar to (1*) in aqueous medium, but as compared with the latter shows no weakening of action in serum. 9-ω-Phenanthridylmethyl-*N*-pyridinium chloride (30*) is among the most active members of the series for both organisms in serum as well as in aqueous medium. 9-ω-Piperidinomethylphenanthridine hydrochloride (31*), however, shows distinct weakening of action in serum as compared with peptone water medium.

In general the presence of a quaternary nitrogen atom as in phenanthridine methiodide (4*; Pictet and Ankersmit, *loc. cit.*) leads to distinct enhancement of action in serum. Antiseptic properties are not further greatly affected by the presence in addition of an amino-group in the 3-position as in 3-amino-9 : 10-dimethylphenanthridinium chloride (5; J., 1932, 2230) or of an acetamido-group (6 and 7).

The compounds in which an aminophenyl group is attached in the 9-position (8—23) exhibit certain definite relations between constitution and action.

These are well exemplified in the series which has in addition an amino-group in the 3-position. 3-Amino-9-*p*-aminophenylphenanthridine sulphate (18*) is only moderately antiseptic for either organism in peptone water medium and acts less well in serum, being practically equal to (1*). The corresponding quaternary chloride (20*) is very powerfully antiseptic for *Staphylococcus* both in peptone water and in serum and also for *B. coli* in serum. As compared with this, the acetamido-derivative (19*) is greatly reduced in action.

† Work done with the support of the Medical Research Council in the Department of Bacteriology and Pathology, the University and Western Infirmary, Glasgow.

‡ The compounds to the numbers of which an asterisk is attached are given in the table showing antiseptic values.

The series with an amino-group in the 7-position (21—23) possesses respectively activities of nearly the same order as those just mentioned, and shows the same relations between constitution and action. With the 9-aminophenyl compounds lacking substituents in the phenanthridine nucleus (8—14), the results are obscured by the very slight solubility of the phenanthridine salts (8* and 9) in peptone water—less than 1 : 40,000, although a solution of 1 : 1000 is obtained in serum; but the same relations hold here, the quaternary compounds being much the most active (cf. 8* and 10*) and the acetamido-derivative of the latter again being less strongly antiseptic. The 9-*o*-, -*m*- and -*p*-aminophenyl-10-methylphenanthridinium chlorides (13, 14, 10*; J., 1931, 2454) do not differ much in potency among themselves, the last being slightly the most active. The substitution of a dimethylamino- for an amino-group in the last-named causes no striking increase in antiseptic activity when the nitrogen atom is either tertiary (8*, 9) or quaternary (10* and 11* compared with 15* and 16*). On the other hand, the diquaternary compound (17*) is very weak, except in its action on *B. coli* in serum.

As regards the relations between chemical constitution and biological action, certain of the facts established in the present work have analogies in other series. Thus the enhanced antiseptic action of the quaternary salts of the series as compared with the analogous compounds in which the nitrogen atom is tervalent, was also observed with the less powerfully antiseptic members of the acridine series, *e.g.*, 9-phenylacridine and 2 : 7-tetraethyldiaminoacridine (Browning, Cohen, Gaunt, and Gulbransen, *loc. cit.*). Also the effect of acetylation of an amino-group in markedly diminishing antiseptic action has been paralleled in the acridine series (*loc. cit.*), and the same holds for acetylation of the amino-group in the benzene nucleus of quaternary salts of amino-derivatives of styryl- and anil-quinolines (Browning, Cohen, Ellingworth, and Gulbransen, *loc. cit.*). The failure of compounds containing a secondary or tertiary group to show distinct superiority over that containing the corresponding primary amino-group has also been observed in the acridine series, although with the styryl and anil compounds the introduction of methyl or ethyl radicals into the amino-group of the benzene nucleus tends to enhance their antiseptic properties, and a similar result follows in the triphenylmethane dyes.

All the compounds in the present work have been tested for chemotherapeutic action in mice infected experimentally with trypanosomes. Only Nos. 19 and 23 are effective, the latter in infections with *T. brucei* and *T. congolense*, the former sterilising *T. brucei* only (Browning, Morgan, Robb, and Walls, *J. Path. Bact.*, 1938, **46**, 203).

*Table of Antiseptic Values.*

| Substance No. | Antiseptic action.* *Staphylococcus.* P. | S. | *B. coli.* P. | S. | Precipitation.† P. | S. |
|---|---|---|---|---|---|---|
| 1 | 4 | <1 | 4 | <1 | 4 | <1 |
| 4 | 4 | 20 | 4 | 100 | — | — |
| 8 | <1 | <1 | <1 | 1 | 40 | 2 |
| 10, 11 | 40 | 100 | 2 | 100 | — | — |
| 15, 16 | 200 | 200 | 10 | 40 | — | — |
| 17 | 1 | 10 | 2 | 100 | — | — |
| 18 | 4 | <1 | 2 | <1 | 4 | — |
| 19 | <1 | 20 | <1 | 4 | 4 | 4 |
| 20 | 200 | 100 | 4 | 100 | — | — |
| 29 | 10 | 10 | 1 | 10 | — | — |
| 30 | 40 | 40 | 10 | 40 | — | — |
| 31 | 40 | 4 | 4 | 2 | 2 | — |

* Antiseptic action: the numbers are the reciprocals ÷ 1000 of the lowest concentrations which suffice to produce inhibition of growth in 48 hours at 37°.

† Precipitation: the numbers are the reciprocals ÷ 1000 of the lowest concentrations (below 1 : 1000) which cause precipitation in the medium.

P = peptone water medium. S = ox serum previously heated at 56°.

## EXPERIMENTAL.

3-*Amino-9-methylphenanthridine hydrochloride* (2) crystallised from a solution of the base (I) in dilute hydrochloric acid in minute yellow needles (Found: loss at 100°, 13·1; Cl, 12·4. $C_{14}H_{12}N_2,HCl,2H_2O$ requires $H_2O$, 12·85; Cl, 12·65%).

3-*Dimethylamino-9-methylphenanthridine* (I).—The product of the reaction between the primary amine (3 g.) and methyl iodide (6 g.) at 150° for 6 hours was extracted with hot dilute hydrochloric acid. The red extract was neutralised with potassium carbonate, and heated on

the steam-bath until a brown crystalline solid was formed; this was recrystallised from alcohol, forming large, transparent, brown prisms (2 g.), m. p. 146° (Found : C, 81·3; H, 6·75; N, 12·15. $C_{16}H_{16}N_2$ requires C, 81·35; H, 6·8; N, 11·85%). Evaporation of a solution of the *base* in dilute hydrochloric acid (1 equiv.) left a crystalline mass, which gave small red needles of the *hydrochloride* (3) from alcohol; the salt was very soluble in water, but sparingly so in alcohol (Found : Cl, 12·85. $C_{15}H_{14}N_2$,HCl requires Cl, 13·0%).

3-*Acetamido*-9 : 10-*dimethylphenanthridinium Chloride* (6).—When an aqueous solution of the methosulphate (J., 1932, 2230) was treated with potassium iodide, the *iodide* (7) crystallised in yellow needles (Found : I, 32·05. $C_{17}H_{17}ON_2I$ requires I, 32·4%). The iodide was refluxed in aqueous methyl alcohol with silver chloride for 4 hours; after filtration and evaporation to small bulk, ether was added, which precipitated the *chloride* (6) in pale yellow needles (Found : loss at 100°, 5·35; Cl, 11·1. $C_{17}H_{17}ON_2Cl,H_2O$ requires $H_2O$, 5·65; Cl, 11·15%).

9-p-*Aminophenylphenanthridine Hydrochloride* (8).—The base (II; R = H) was dissolved in hot dilute hydrochloric acid, and ammonia added until red prisms of the *monohydrochloride* separated (Found : Cl, 11·4. $C_{19}H_{14}N_2$,HCl requires Cl, 11·6%).

9-p-*Dimethylaminophenylphenanthridine* (II; R = Me).—The primary amine (3 g.) was methylated by methyl iodide (6 g.) at 150°. After 8 hours the product was extracted with dilute hydrochloric acid. Sodium carbonate was added to the hot solution, and after 1 hour on the steam-bath the precipitate was extracted with benzene. By evaporation of the solvent, the *tertiary amine* was obtained in buff prisms (2 g.), m. p. 179—181°, which were very soluble in benzene, but more sparingly so in alcohol (Found : C, 84·4; H, 5·95; N, 9·75. $C_{21}H_{18}N_2$ requires C, 84·55; H, 6·05; N, 9·4%). The *hydrochloride* (9) crystallised from water in hydrated orange-red transparent plates (Found for salt dried at 100° : Cl, 10·3. $C_{21}H_{18}N_2$,HCl requires Cl, 10·6%).

9-p-*Aminophenyl*-10-*methylphenanthridinium iodide* (11) was obtained in the usual way from the chloride (J., 1931, 2456) in ruby-red transparent prisms (Found : I, 30·1. $C_{20}H_{17}N_2I$ requires I, 30·8%).

9-p-*Acetamidophenyl*-10-*methylphenanthridinium chloride* (12), obtained from the methosulphate (*loc. cit.*), crystallised from its neutral aqueous solution in pale orange prisms (Found : loss at 100°, 9·25. $C_{22}H_{19}ON_2Cl,2H_2O$ requires $H_2O$, 9·05%. Found for dry salt : Cl, 9·7. $C_{22}H_{19}ON_2Cl$ requires Cl, 9·8%).

9-p-*Dimethylaminophenyl*-10-*methylphenanthridinium Iodide* (15) (III; R = Me).—When a solution of the relevant tertiary amine (II; R = Me) (2 g.) in nitrobenzene (20 c.c.) at *ca.* 180° was treated with methyl *p*-toluenesulphonate (1·4 g.; > 1 equiv.), the solution became dark red and heat was evolved. On cooling, there separated a white *p*-toluenesulphonate (0·5 g.), which was purified by crystallisation from alcohol and then converted into the iodide. The product, 9-*phenanthridyl*-p-*phenyltrimethylammonium iodide* (IV), crystallised from water or alcohol in white plates, m. p. 179° (decomp.), but the red melt resolidified and then melted a 235°; it had evidently been converted into its isomeride (III; R = Me) (Found for whit iodide; C, 60·15; H, 4·65; N, 6·15; I, 28·8. $C_{22}H_{21}N_2I$ requires C, 60·0; H, 4·75; N, 6·35; I 28·85%).

The red aqueous liquor left after steam distillation of nitrobenzene deposited, on coolin orange prisms of 9-p-*dimethylaminophenyl*-10-*methylphenanthridinium* p-*toluenesulphona* (compare III) (1·2 g.), which melted with loss of water at 120° and then set to a dark red gla (Found : C, 67·35; H, 6·15; N, 5·65; S, 6·35; loss at 100°, 6·85. $C_{29}H_{28}O_3N_2S,2H_2O$ requir C, 67·0; H, 6·15; N, 5·4; S, 6·15; $H_2O$, 6·9%). The *iodide* (16) formed small brick-red prism m. p. 238° (decomp.) (Found : C, 59·55; H, 5·1; N, 6·8; I, 28·55. $C_{22}H_{21}N_2I$ requires C, 60· H, 4·75; N, 6·35; I, 28·85%). The *chloride* (15), which was prepared from the iodide, was ve soluble in water and alcohol, but crystallised from the former in hydrated ruby-red prisn which had copper reflex (Found for salt dried at 100° : N, 8·25; Cl, 10·1. $C_{22}H_{21}N_2Cl$ requi N, 8·05; Cl, 10·2%).

When methyl sulphate was used as methylating agent, the salt that separated from t nitrobenzene was the diquaternary dimethosulphate, characterised by the *di-iodide* (17) ( which crystallised from water in transparent, pale yellow prisms, m. p. 232—236° (decom (Found : C, 48·1; H, 4·2; N, 4·85; I, 43·3. $C_{23}H_{24}N_2I_2$ requires C, 47·45; H, 4·1; N, 4 I, 43·65%). The same salt was obtained in high yield when a large excess of methyl *p*-tolue sulphonate was used. On cooling, the nitrobenzene filled with white deliquescent plates of diquaternary di-*p*-toluenesulphonate, which was readily converted into the foregoing di-iod The white chloride obtained from this salt lost methyl chloride slowly at 100° to yield the monochloride.

*Methylation of* 9-p-*Aminophenyl*-10-*methylphenanthridinium Iodide*.—The quaternary salt (2 g.) and methyl iodide (4 g.), after being heated at 180° for 7 hours, gave a product, from a hot aqueous extract of which a brick-red iodide separated on cooling (0·5 g.). It was characterised as 9-*p*-dimethylaminophenyl-10-methylphenanthridinium iodide by conversion into the orange prisms of the *p*-toluenesulphonate by means of silver *p*-toluenesulphonate. The aqueous mother-liquor from which the red iodide separated gave on evaporation characteristic crystals of the diquaternary di-iodide (V).

5-*Nitro*-2-p-*nitrobenzamidodiphenyl*, obtained by the condensation of 5-nitro-2-aminodiphenyl (10 g.) and *p*-nitrobenzoyl chloride (10 g.) in hot pyridine (40 c.c.), crystallised from glacial acetic acid in buff prisms (11·5 g.), m. p. 209° (Found : N, 11·4. $C_{19}H_{13}O_5N_3$ requires N, 11·55%).

3-*Nitro*-9-p-*nitrophenylphenanthridine*.—The foregoing compound (20 g.) was refluxed with phosphorus oxychloride (40 g.) for 30 hours. The product left after cautious decomposition with water crystallised from boiling pyridine in pale yellow, felted needles (11·5 g.), m. p. 294°, very sparingly soluble in all other solvents (Found : N, 12·35. $C_{19}H_{11}O_4N_3$ requires N, 12·15%). When the residue left after evaporation of pyridine was again treated with phosphorus oxychloride, a further yield (2 g.) was obtained.

3-*Amino*-9-p-*aminophenylphenanthridine* was obtained by reduction of the foregoing compound (11·5 g.) in alcoholic solution (350 c.c.) in an autoclave with hydrogen (5 atms.) at 50°, platinic oxide being used as catalyst. The almost colourless, prismatic needles (8·5 g.), m. p. 233°, were sparingly soluble in alcohol (Found : C, 79·6; H, 5·4; N, 14·95. $C_{19}H_{15}N_3$ requires C, 80·0; H, 5·25; N, 14·75%). The *hydrobromide* crystallised from its dark red aqueous solution in clusters of orange plates (Found : loss at 100°, 4·8; Br, 20·2. $C_{19}H_{16}N_3Br,H_2O$ requires $H_2O$, 4·7; Br, 20·85%). The sparingly soluble *sulphate* crystallised in cream-coloured needles (Found after drying at 100° : N, 10·8; S, 8·1. $C_{19}H_{15}N_3,H_2SO_4$ requires N, 10·95; S, 8·35%).

The dark red solution of the amine in glacial acetic acid was readily acetylated by acetic anhydride. The *diacetyl* compound crystallised in white felted needles, m. p. 327—328° (decomp.) (Found : C, 74·7; H, 5·25; N, 11·5. $C_{23}H_{19}O_2N_3$ requires C, 74·8; H, 5·15; N, 11·4%).

3-*Acetamido*-9-p-*acetamidophenyl*-10-*methylphenanthridinium chloride* (19) was prepared by methylation of the foregoing compound (5 g.) in hot nitrobenzene (100 c.c.) with methyl *p*-toluenesulphonate (3 g.). The quaternary salt crystallised from the aqueous liquor left after steam-distillation of nitrobenzene in clumps of pale orange needles. The *chloride* (4 g.) was salted out from the hot solution in small, pale yellow needles, sparingly soluble in water to a neutral solution (Found : N, 9·95; Cl, 8·1. $C_{24}H_{22}O_2N_3Cl$ requires N, 10·0; Cl, 8·45%).

3-*Amino*-9-p-*aminophenyl*-10-*methylphenanthridinium Chloride* (20) (X).—The foregoing salt (4 g.) was readily hydrolysed by boiling concentrated hydrochloric acid (20 c.c.). On neutralisation of the solution, the *quaternary* salt crystallised in transparent, red, prismatic needles (2·6 g.), fairly soluble in water (Found : C, 69·1; H, 5·35; loss at 100°, 2·4, 2·6. $C_{20}H_{18}N_3Cl,0·5H_2O$ requires C, 69·65; H, 5·5; $H_2O$, 2·6%. Found for salt dried at 100° : N, 12·6; Cl, 10·45. $C_{20}H_{18}N_3Cl$ requires N, 12·5; Cl, 10·6%).

The following compounds were prepared in substantially the same way as their isomerides.

4′-*Nitro*-2-p-*nitrobenzamidodiphenyl* crystallised from glacial acetic acid in white prisms, m. p. 208° (Found : N, 11·95. $C_{19}H_{13}O_5N_3$ requires N, 11·55%).

7-*Nitro*-9-p-*nitrophenylphenanthridine*.—The foregoing compound (28 g.) was dehydrated less readily than its isomeride, the yield after 30 hours' refluxing being 8 g.; by repeated re-treatment of the residue a further 8·5 g. were obtained. Almost white, felted needles, m. p. 327°, crystallised from pyridine (Found : N, 12·4. $C_{19}H_{11}O_4N_3$ requires N, 12·15%).

7-*Amino*-9-p-*aminophenylphenanthridine* crystallised from alcohol in pale yellow, transparent cubes, m. p. 212° (Found : C, 79·8; H, 5·3; N, 14·85. $C_{19}H_{15}N_3$ requires C, 80·0; H, 5·25; N, 14·75%). The red hydrochloride was extremely soluble in water, but the *sulphate* (21) was obtained in brick-red talc-like crystals (Found for salt dried at 100° : N, 10·95; S, 8·35. $C_{19}H_{15}N_3,H_2SO_4$ requires N, 10·95; S, 8·35%). The *diacetyl* compound crystallised from alcohol in solvated colourless prisms, m. p. 172—173° (Found after drying at 100° : N, 11·35. $C_{23}H_{19}O_2N_3$ requires N, 11·4%).

7-*Acetamido*-9-p-*acetamidophenyl*-10-*methylphenanthridinium* p-*toluenesulphonate* crystallised from water or alcohol in yellow felted needles, or in transparent prisms (Found : N, 7·7. $C_{31}H_{29}O_5N_3S$ requires N, 7·55%). The *chloride* (22) formed yellow prisms from alcohol, m. p. 231° (decomp.) (Found : C, 64·65; H, 5·7; N, 9·7; Cl, 7·8; loss at 100° 5·3. $C_{24}H_{22}O_2N_3Cl,1·5H_2O$ requires C, 64·5; H, 5·6; N, 9·4; Cl, 7·95; $H_2O$, 6·05%).

*7-Amino-9-p-aminophenyl-10-methylphenanthridinium chloride* (23) crystallised from water ruby-red transparent plates, m. p. 262° (decomp.), but dependent on rate of heating (Found: 69·35; H, 5·3; 5·5; loss at 120°, 2·3. $C_{20}H_{18}N_3Cl,0\cdot5H_2O$ requires C, 69·65; H, 5·5; $H_2O$, ·6%. Found for salt dried at 120°: N, 12·4; Cl, 10·4. $C_{20}H_{18}N_3Cl$ requires N, 12·5; Cl, 0·6%).

*4'-Nitro-2-benzamidodiphenyl*.—4'-Nitro-2-xenylamine (3 g.) and benzoic anhydride (3·5 g.) were heated at 150° for 1 hour. The product was lixiviated with hot dilute alkali; it then crystallised from alcohol in colourless acicular prisms (4 g.), m. p. 165·5° (Found: N, 8·85. $C_{19}H_{14}O_3N_2$ requires N, 8·8%).

*7-Nitro-9-phenylphenanthridine* was obtained by fractional crystallisation from glacial acetic acid of the product of 7 hours' reaction of the foregoing (3·5 g.) and phosphorus oxychloride. It crystallised in flocculent, pale yellow needles (0·8 g.), m. p. 237° (Found: N, 9·4. $C_{19}H_{12}O_2N_2$ requires N, 9·35%).

*5 : 4'-Dinitro-2-benzamidodiphenyl*, obtained from 5 : 4'-dinitro-2-xenylamine (Scarborough and Waters, J., 1927, 89) and benzoic anhydride by the method previously described, crystallised from nitrobenzene in white plates, m. p. 250° (Found: N, 12·0. $C_{19}H_{13}O_5N_3$ requires N, 11·55%). After prolonged heating with phosphorus oxychloride, the yield of *3 : 7-dinitro-9-phenylphenanthridine* was very small; by fractional crystallisation of the product from glacial acetic acid and benzene it was obtained in flat yellow plates, m. p. 275—277° (Found: N, 12·4. $C_{19}H_{11}O_4N_3$ requires N, 12·2%).

*9-Methylaminophenanthridine* (XIII; R = H, R' = Me).—The product of the reaction between 9-chlorophenanthridine (5 g.) and methylamine (10 g. of 33% alcoholic solution) at 180° for 5 hours was extracted with dilute sulphuric acid. On neutralisation of the extract the amine was obtained in quantitative yield; it crystallised from alcohol in colourless prismatic needles, m. p. 187° (Found: N, 13·55. $C_{14}H_{12}N_2$ requires N, 13·45%). The hydrochloride was very sparingly soluble in water, but the *sulphate* (25) crystallised in hydrated needles, the 2% aqueous solution of which had $p_H$ 6—6·5 (Found for salt dried at 100°: S, 6·0. $C_{14}H_{12}N_2,0\cdot5H_2SO_4$ requires S, 6·2%). The *acetyl* compound was obtained quantitatively when the base was refluxed with acetic anhydride and fused sodium acetate; it crystallised from aqueous methyl alcohol in white plates, m. p. 155° (Found: N, 11·45. $C_{16}H_{14}ON_2$ requires N, 11·2%).

*9-Dimethylaminophenanthridine* (XIII; R = R' = Me), prepared in the same way as the foregoing compound by means of dimethylamine, crystallised from a small volume of light petroleum (b. p. 60—80°) in colourless prisms, m. p. 61·5° (Found: N, 12·35. $C_{15}H_{14}N_2$ requires N, 12·6%). The *hydrochloride* (26) occurred in hydrated white needles, the 2% aqueous solution of which had $p_H$ 4·5—5 (Found for salt dried at 100°: Cl, 13·5. $C_{15}H_{14}N_2,HCl$ requires Cl, 13·7%).

*9-Phenanthridyltrimethylammonium iodide* (27) (XIV) was obtained in moderate yield by the reaction between 9-chlorophenanthridine and alcoholic trimethylamine. When an aqueous extract of the product was treated with potassium iodide, the white salt crystallised, m. p. 234° (decomp.), $p_H$ of 2% aqueous solution 5·5 (Found: I, 34·9. $C_{16}H_{17}N_2I$ requires I, 34·9%).

*9-Dimethylamino-10-methylphenanthridinium Iodide* (28) (XV).—9-Dimethylaminophenanthridine (2 g.) and methyl iodide (2 g.) were heated at 125° for 4 hours. When a hot aqueous extract of the product was cooled, the quaternary *iodide* crystallised in yellow needles (1·7 g.), m. p. 230° (efferv.) (Found: N, 7·55; I, 35·2. $C_{16}H_{17}N_2I$ requires N, 7·7; I, 34·9%). When the aqueous solution, which had a neutral reaction, was heated, smooth decomposition occurred slowly with separation of a non-basic colourless oil, which solidified on cooling to white needles m. p. 112° alone or in admixture with *N*-methylphenanthridone (Graebe and Wander, *Annalen* 1893, **276**, 245).

*9-ω-Phenanthridylmethyltrimethylammonium Iodide* (29).—When an aqueous extract of the product of the reaction between 9-ω-chloromethylphenanthridine and trimethylamine at 100 for 2 hours was treated with potassium iodide, the *iodide* was precipitated in colourless prism m. p. *ca.* 222° (decomp.), dependent on the rate of heating. Its aqueous solution was neutr (Found: I, 33·3. $C_{17}H_{19}N_2I$ requires I, 33·6%).

*9-ω-Phenanthridylmethyl-N-pyridinium chloride* (30), prepared similarly from pyridin crystallised from water in colourless plates, decomp. *ca.* 250° (Found: N, 8·65; Cl, 10·85; lo at 100°, 5·45, 5·2. $C_{19}H_{15}N_2Cl,H_2O$ requires N, 8·2; Cl, 10·95; $H_2O$, 5·55%). The 2% aqueo solution had $p_H$ 6·5. The corresponding nitrate, sulphate, and perrhenate were very sparing soluble in water.

*9-ω-Piperidinomethylphenanthridine* (31).—9-ω-Chloromethylphenanthridine (4·5 g.) ar

piperidine (6 g.) reacted at 100° with evolution of heat. The product (3·2 g.) crystallised from light petroleum (b. p. 60—80°) in pale yellow rhombs, m. p. 90—93° (Found: N, 10·3. $C_{15}H_{20}N_2$ requires N, 10·15%). The hydrochloride separated from aqueous solution (2% had $p_H$ 5·5) in white prisms (Found: Cl, 10·75. $C_{15}H_{20}N_2,HCl,H_2O$ requires Cl, 10·75%).

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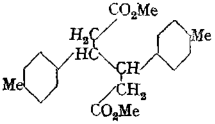
## 79. *Symmetrical Derivatives of Chrysene. Part I.*

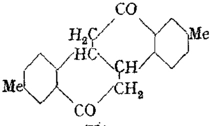
By G. R. RAMAGE.

The double ring closure of substituted diphenyladipic acids to give symmetrical chrysene derivatives has been extended, and 5 : 14-dimethylchrysene is now described. Of particular interest is the preparation of dimethylhexahydrochrysenes (VI), having two angle methyl groups in *cis*- and *trans*-positions, and the selenium dehydrogenation of these is to be investigated.

IN the early stages of attempts to synthesise substances related to the sex-hormones, Ramage and Robinson (J., 1933, 607) employed a method of possible general application for the preparation of symmetrical chrysene derivatives. It was shown that *meso*- and *r*-βγ-diphenyladipic acids could be converted into *trans*- and *cis*-hexahydrochrysenes respectively, and the corresponding series from βγ-dianisyladipic acids was completed later (Lewis, Ramage, and Robinson, J., 1935, 1412). The method appears to be suitable for the preparation of chrysene homologues and 5 : 14-dimethylchrysene has now been synthesised. *p*-Tolualdehyde was condensed with methyl acetate and the resulting crystalline methyl *p*-methylcinnamate was reduced in ethereal solution by amalgamated aluminium. About half formed bimolecular product, which was separated by ether into pure crystalline *methyl* βγ-*di*-p-*tolyladipate*-a (I) and the crude isomer-*b*. These by analogy with the diphenyladipic acid series represent the *meso*- and the racemic form respectively. Ring closure of βγ-*di*-p-*tolyladipic*-a *acid* was effected with sulphuric acid, or by the Friedel–Crafts reaction on the acid chloride. The *b*-form was similarly cyclised by the Friedel–Crafts reaction. The resulting 2 : 11-*diketo*-5 : 14-*dimethylhexahydrochrysene*-a and -b (II) gave on reduction the corresponding two forms of the *hydrocarbon* (III), both of which were smoothly dehydrogenated by selenium to 5 : 14-*dimethylchrysene*, m. p. 218°, characterised by a *trinitrobenzene* derivative, m. p. 195°, a *picrate*, m. p. 171—172°, and a *styphnate*, m. p. 204°. These derivatives are quite stable, whereas only a trinitrobenzene compound from chrysene can be prepared and 2 : 11-dimethylchrysene failed to give a picrate (J., 1935, 1414).



(I.)



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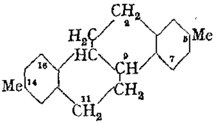
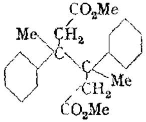


(III.)

An interesting extension of the work followed from the aluminium reduction of methyl β-methylcinnamate, although the substituted adipic esters (IV) were isolated in very poor yield. These on ring closure with sulphuric acid gave 2 : 11-*diketo*-9 : 18-*dimethylhexahydrochrysene*-a and -b (V), but for the first time in this series difficulty was experienced with the reduction of the carbonyl groups. The ordinary Clemmensen reduction or its modification by the addition of solvent gave solid products, higher melting than the original ketones, dissolving only in pyridine, and considered to be the corresponding alcohols.

Clemo and Metcalfe (J., 1937, 1520) have recently drawn attention to, and discussed similar unusual behaviour in the Clemmensen reduction. Attempts were therefore made to find an alternative procedure, and the more readily available methyl *r*-diphenyladipate was submitted to a Bouveault reduction, but the glycol isolated in low yield was not cyclised to *cis*-hexahydrochrysene by phosphoric oxide in xylene. On the other hand, although the Wolff reduction of the semicarbazones of *cis*- and *trans*-diketohexahydrochrysenes gave non-crystallisable gums, from the *hydrazones*, *cis*- and *trans*-hexahydrochrysene were isolated in good yield. By applying the latter method to the two forms of (V), 9 : 18-*dimethylhexahydrochrysene*-a, m. p. 144°, and -b (VI), m. p. 105°, were obtained and it is proposed to examine the selenium dehydrogenation of these substances, which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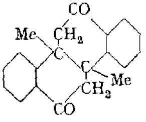
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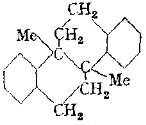
(VI.)

contain angle methyl groups presumably in *trans*- and *cis*-positions respectively. Preliminary experiments on the small amounts of hydrocarbons available show that at 360° dehydrogenation is very slow, but following prolonged heating, chrysene has been isolated together with derivatives of either a methyl- or dimethyl-chrysene. This result is in accord with previously observed migration or elimination of angle methyl groups under such treatment.

## EXPERIMENTAL.

*Methyl* p-*Methylcinnamate*.—*p*-Tolualdehyde (11 g.) and anhydrous methyl acetate (50 c.c.) were added to powdered sodium (2·1 g.) and heated for 1 hour on the water-bath with occasiona shaking. The mixture was treated with dilute hydrochloric acid, and the ester layer dried anc fractionated, giving a colourless oil (12·5 g.), b. p. 145—165°/22 mm. After addition of an equa volume of methyl alcohol, methyl *p*-methylcinnamate (10·5 g.) crystallised on strong cooling an had m. p. 57—58°, b. p. 157°/22 mm.

βγ-*Di*-p-*tolyladipic*-a *Acid*.—The above crystalline ester (50 g.), dissolved in ether (1·5 l. was poured on amalgamated aluminium foil (100 g.) (J., 1930, 2148), and water (40 c.c.) adde with cooling in running water and frequent shaking during 8 hours. The ether was filter and combined with washings from the aluminium sludge, and, after evaporation of t ether, methyl β-*p*-tolylpropionate (23 g.), b. p. 132°/20 mm., was removed by distillati as a colourless oil which solidified on standing, m. p. 39° (Found : C, 74·2; H, 7·8. Calc C, 74·2; H, 7·8%). The undistilled residue with ether gave an insoluble portion, from whic by crystallisation from methyl alcohol, *methyl* βγ-*di*-p-*tolyladipate*-a (9·0 g.) was obtained colourless needles, m. p. 150° (Found : C, 75·0; H, 7·2. $C_{22}H_{26}O_4$ requires C, 74·6; H, 7·3% On hydrolysis with aqueous-alcoholic potassium hydroxide βγ-*di*-p-*olyladipic*-a *acid* v obtained in almost quantitative yield; it crystallised from butyl alcohol in small prisı m. p. 320° (Found : C, 73·8; H, 6·8. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·7%). A further sn quantity (0·7 g.) of this acid was obtained by dissolving the aluminium sludge in hydrochl acid. From the ethereal mother-liquor, crude methyl βγ-di-*p*-tolyladipate-*b* (18 g.) recovered.

2 : 11-*Diketo*-5 : 14-*dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-a (II).—Di-*p*-tolyladi *a* acid (2·0 g.) and purified thionyl chloride (5 c.c.) were refluxed (1 hour), the excess of solv removed from the clear solution, and the powdered solid residue, in dry tetrachloroetl (20 c.c.), treated with powdered aluminium chloride (4 g.), slowly warmed to 60° with shak and maintained at this temperature for 12 hours. The solvent was steam-distilled, and alkali-insoluble *diketodimethylhexahydrochrysene*-a extracted with boiling anisole or n benzene, which gave, on cooling, long colourless prisms (1·2 g.), m. p. 312° (decomp.) af further crystallisation (Found : C, 82·7; H, 6·3. $C_{20}H_{18}O_2$ requires C, 82·8; H, 6·2%). diketone-*a* (1·8 g.) was also obtained by heating the acid (3·0 g.) with sulphuric acid (40 85%) for 3 hours.

5 : 14-*Dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-a (III).—The above diketone (1·0 g.), anisole (20 g.), amalgamated zinc (70 g.), and concentrated hydrochloric acid (10 c.c.) were refluxed for 36 hours with two additions of acid (5 c.c.) at 12-hour intervals. The anisole layer was separated, the solvent removed, and the residue distilled under reduced pressure; *dimethylhexahydrochrysene*-a (0·65 g.) crystallised from ethyl alcohol in long needles, m. p. 140° (Found: C, 91·6; H, 8·4. $C_{20}H_{22}$ requires C, 91·6; H, 8·4%).

2 : 11-*Diketo*-5 : 14-*dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-b (II).—The crude ether-soluble ester (18 g.) obtained in the reduction above was hydrolysed and gave a solid acid mixture, precipitated by ice; this was dried, and the sticky product cyclised through its acid chloride as described for the diketone-*a*. The alkali-insoluble material was extracted with boiling anisole, which, on cooling, gave the diketone-*a* (0·7 g.); after removal of the solvent, *diketodimethylhexahydrochrysene*-b solidified in contact with ethyl alcohol and crystallised from butyl alcohol in almost colourless plates (4·4 g.), m. p. 193—194°, raised to 201—202° by distillation under reduced pressure and a further crystallisation (Found: C, 82·7; H, 6·1. $C_{20}H_{18}O_2$ requires C, 82·8; H, 6·2%).

5 : 14-*Dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-b (III).—The diketone-*b* (1·0 g.), by a Clemmensen reduction without anisole, gave *dimethylhexahydrochrysene*-b, which solidified after distillation under reduced pressure (0·6 g.) and crystallised from ethyl alcohol in colourless plates, m. p. 108° (Found: C, 91·4; H, 8·3. $C_{20}H_{22}$ requires C, 91·6; H, 8·4%).

5 : 14-*Dimethylchrysene*.—Either dimethylhexahydrochrysene-*a* or -*b* (0·5 g.) was dehydrogenated in 6 hours by heating with selenium (1·5 g.) at 280°, raised to 320°, the sublimate being repeatedly melted and returned down the tube. The *dimethylchrysene* (0·4 g.) was sublimed from the selenium under reduced pressure, then from sodium; it crystallised from benzene in large plates, m. p. 218° (Found: C, 93·9; H, 6·0. $C_{20}H_{16}$ requires C, 93·8; H, 6·2%).

The 1 : 3 : 5-*trinitrobenzene* compound, prepared in benzene solution, crystallised from this solvent in yellow needles, m. p. 195° (Found: N, 9·3. $C_{20}H_{16},C_6H_3O_6N_3$ requires N, 9·0%). The *styphnate* crystallised in orange needles, m. p. 204° (Found: N, 8·5. $C_{20}H_{16},C_6H_3O_8N_3$ requires N, 8·4%), and the *picrate* in red needles, m. p. 171—172° (Found: N, 8·8. $C_{20}H_{16},C_6H_3O_7N_3$ requires N, 8·7%), both from benzene.

*General Procedure in Wolff Reductions*.—The diketone (1·0 g.), hydrazine hydrate (2 c.c. of 50%), and absolute alcohol (100 c.c.) were refluxed over-night, most of the alcohol distilled, and the hydrazone precipitated by cooling and dilution with water if necessary. The hydrazone (1·0 g.) and sodium ethoxide (0·5 g. of sodium in 8 c.c. of absolute alcohol) were heated for 15 hours at 180°, the solution extracted with ether, the extract washed with water and dried, the solvent removed, and the residual oil crystallised from alcohol.

1 : 2 : 9 : 10 : 11 : 18-*Hexahydrochrysene*.—*cis*-Diketohexahydrochrysene (1·0 g.) (J., 1933, 609) gave a *dihydrazone*, which crystallised from aqueous alcohol in fine needles, decomp. about 120° (Found: N, 19·6. $C_{18}H_{18}N_4$ requires N, 19·3%), and from which *cis*-hexahydrochrysene (0·3 g.), m. p. 79°, identical with the product from a Clemmensen reduction, was obtained.

The *dihydrazone* from *trans*-diketohexahydrochrysene (1·0 g.) (J., 1933, 608) crystallised from quinoline in needles, m. p. 360° (Found: N, 19·3. $C_{18}H_{18}N_4$ requires N, 19·3%). It was converted as above into *trans*-hexahydrochrysene (0·4 g.), m. p. 112°.

*Aluminium Reduction of Methyl β-Methylcinnamate*.—From methyl bromoacetate (500 g.), by the method of v. Auwers (*Annalen*, 1917, **413**, 272), methyl β-methylcinnamate (320 g.), b. p. 129—133°/12 mm., was obtained (Found: C, 74·6; H, 6·9. Calc.: C, 75·0; H, 6·8%); this was reduced in five separate experiments, in each of which prepared aluminium foil (100 g.) was used. After removal of the ether, the combined residues were distilled and gave methyl β-phenyl-*n*-butyrate (270 g.), b. p. 120—122°/15 mm. (Found: C, 74·1; H, 7·8. Calc.: C, 74·2; H, 7·8%). The residual gum (30 g.), treated with methyl alcohol, partly crystallised, giving *methyl βγ-diphenyl-βγ-dimethyladipate*-a (5·5 g.), m. p. 134° (Found: C, 74·9; H, 7·3. $C_{22}H_{26}O_4$ requires C, 74·6; H, 7·3%); the mother-liquor contained the methyl ester-*b*, which was not further purified.

2 : 11-*Diketo*-9 : 18-*dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-a (V).—The above ester-*a* (1·0 g.), concentrated sulphuric acid (12 c.c.), and water (4 c.c.) were heated on the water-bath for 3 hours. On cooling and dilution with water, the *diketodimethylhexahydrochrysene*-a was precipitated; after filtration and digestion with sodium carbonate solution, it crystallised from pyridine in prisms (0·7 g.), m. p. 256° (Found: C, 82·7; H, 6·0. $C_{20}H_{18}O_2$ requires C, 82·8; H, 6·2%).

2 : 11-*Diketo*-9 : 18-*dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-b (V).—The above methyl ester-*b*, recovered from the mother-liquor, was treated in 2-g. portions with sulphuric

:id as above; the *diketodimethylhexahydrochrysene*-b obtained (7·2 g. in all) crystallised from yridine in large well-formed prisms, m. p. 229° (Found: C, 82·7; H, 6·1%).

9 : 18-*Dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-a (VI).—The *dihydrazone* from the iketone-*a* (1·0 g.) was not quite pure (Found: N, 16·7. $C_{20}H_{22}N_4$ requires 17·6%), but gave *imethylhexahydrochrysene*-a (0·6 g.) by the Wolff reduction; this was purified by distillation .nder reduced pressure from potassium, followed by crystallisation from ethyl alcohol, giving :olourless prisms, m. p. 144° (Found: C, 91·8; H, 8·3. $C_{20}H_{22}$ requires C, 91·6; H, 8·4%).

9 : 18-*Dimethyl*-1 : 2 : 9 : 10 : 11 : 18-*hexahydrochrysene*-b (VI).—The diketone-*b* (1·0 g.) gave a *dihydrazone*, which crystallised from xylene in fine needles, m. p. 232—234° (decomp.) (Found: N, 17·4. $C_{20}H_{22}N_4$ requires N, 17·6%). This was converted into *dimethylhexahydrochrysene*-b (0·5 g.), which was distilled from potassium under reduced pressure and crystallised from methyl alcohol, forming fine needles, m. p. 105—106°. Slow crystallisation from a cold solution gave a second form in prisms, m. p. 101°, which after resolidifying cleared at 105° (Found: C, 91·7; H, 8·4%).

Part of the work was completed in the Dyson Perrins Laboratory, Oxford. The author thanks Prof. P. Robinson, F.R.S., and Prof. J. L. Simonsen, F.R.S., for their interest and encouragement, and the Chemical Society for a research grant.

UNIVERSITY COLLEGE OF NORTH WALES, BANGOR. [*Received, January 26th*, 1938.]

# NOTES.

## 1-*Aza*bicyclo[1 : 2 : 2]*heptane*. By G. R. CLEMO and V. PRELOG.

1-AZA*bicyclo*[1 : 2 : 2]HEPTANE has been synthesised in two ways: by the action of ammonia on 1 : 5-dibromo-3-bromomethylpentane (Prelog and Cerkovnikov, *Annalen*, 1936, **525**, 294) and by intramolecular quaternary salt formation from 4-piperidylcarbinol through the 4-bromomethylpiperidine, which was not isolated (Clemo and Metcalfe, J., 1937, 1523). The former authors described the compound as crystalline, whereas Clemo and Metcalfe obtained an oil. Prelog and Cerkovnikov meanwhile carried out the intramolecular salt-formation of 4-iodomethylpiperidine and obtained the same crystalline product. After exchange of specimens and seeding, it was clear that the difference was due to supercooling, for the product of Clemo and Metcalfe then crystallised and melted at 78—79°. We emphasise these observations, the high m. p. being a characteristic property of such bridged cyclic structures. The ease of formation (75·4% of the theoretical yield) of the strained molecule is noteworthy. A third synthesis of this interesting compound will be described elsewhere.

*4-Iodomethylpiperidine Hydriodide*.—4-Piperidylcarbinol (2 g.), prepared by reduction of synthetic ethyl piperidine-4-carboxylate (Hanousek and Prelog, *Coll. Czech. Chem. Comm.* 1932, **4**, 259), was heated for 4 hours at 100° in a sealed tube with red phosphorus (0·8 g.) an hydriodic acid (6 c.c., 70%) (see Clemo and Metcalfe, *loc. cit.*). Water (25 c.c.) was added, th phosphorus separated from the hot solution, and the filtrate evaporated. On cooling, th white *hydriodide* crystallised (4·74 g.; 77·2%). By further evaporation, more of the whi product was obtained (total yield, nearly theoretical). For analysis it was recrystallised fro acetone–ethyl acetate; m. p. 132—133° (corr.) (Found: N, 3·9. $C_6H_{12}NI,HI$ requires N, 4·0%

1-*Aza*bicyclo[1 : 2 : 2]*heptane*.—4-Iodomethylpiperidine hydriodide (4·5 g.) in water (300 c. was stirred while N/2-sodium hydroxide (256 c.c.) was dropped in during 2½ hours at 45°. Aft cooling, benzenesulphonyl chloride (8 g.) was added during a further ½ hour's stirring. T steam-volatile base neutralised 9·83 c.c. of N-hydrochloric acid (75·4% of the theoretical). T base, isolated in the usual way, crystallised to a camphor-like mass. The m. p. of the vacuu distilled base is higher than recorded in the first publication, *viz.*, 78—79°. The picrate (fr acetone–alcohol) melts at 285° (decomp.) (corr.). The product of Clemo and Metcalfe melt after seeding, at the same temperature.—UNIVERSITY OF DURHAM, KING'S COLLE NEWCASTLE-UPON-TYNE, and UNIVERSITY OF ZAGREB, YUGOSLAVIA. [*Received, February* 1 1938.]

*Crystalline Salts derived from* p-*Aminophenylstibonic Acid.* By WILLIAM H. GRAY and IVAN D. LAMB.

OF the large number of organic antimony compounds prepared in the course of chemotherapeutic investigations, but few, and those of types unsuited to the purpose, have been obtained crystalline. The drugs which have found application in the treatment of kala-azar, such as the diethylamine salt and glucoside of *p*-aminophenylstibonic acid, and the product of interaction of this acid with carbamide (Gray, Trevan, Bainbridge, and Attwood, *Proc. Roy. Soc.* 1931, *B*, **108**, 54), as well as their precursors "stibacetin" (sodium *p*-acetamidophenylstibonate) and *p*-aminophenylstibonic acid, have been obtained hitherto only in an amorphous condition. It is therefore of interest to record the preparation of "stibacetin" and sodium *p*-aminophenylstibonate in crystalline form.

If a concentrated aqueous solution of "stibacetin" is allowed to evaporate slowly at room temperature, the salt separates in micro-crystals, consisting of masses or rosettes of thin needles. These have also been obtained by dissolving the crude "stibacetin" in 2 parts of hot water and allowing the solution to cool. Some batches yield the crystals more readily than others. They form a thick paste and are difficult to filter or wash. They are best isolated by centrifuging and washing with a little water and then with alcohol, and can be recrystallised from slightly less than 2 parts of hot water; the yield is poor. So obtained, the product is nearly colourless, but gives a slightly yellow solution in 2 parts of cold water. It does not melt, but decomposes at about 300°. A trace of the sodium chloride used for salting-out the crude "stibacetin" still remains. This crystalline form is almost identical in composition with ordinary "stibacetin," consisting of complex molecules containing 2—3 acetamidophenylstibonic acid residues to 1 atom of sodium [Found for the air-dried substance: $H_2O$, 13·7. Found for the substance dried at 80° in a vacuum: NaCl, 0·3; C, 29·7; H, 3·2; N, 4·5; Sb, 39·3; Na, 3·2; atomic ratios Sb : N = 1·00; Sb : Na = 2·36. Calc. for $(CH_3\cdot CO\cdot NH\cdot C_6H_4)_3Sb_3O_7HNa$: C, 31·9; H, 2·8; N, 4·7; Sb, 40·4; Na, 2·5. Calc. for $(CH_3\cdot CO\cdot NH\cdot C_6H_4)_2Sb_2O_5HNa$: C, 31·2; H, 2·8; N, 4·6; Sb, 39·5; Na, 3·7%].

Crystalline sodium *p*-aminophenylstibonate is obtained by prolonged treatment of "stibacetin" with alkali. The ambiguity in the published accounts with regard to the time required for the completion of this hydrolysis has been mentioned elsewhere (Gray, Trevan, Bainbridge, and Attwood, *loc. cit.*, p. 59). When "stibacetin" (27 g.) in 7% sodium hydroxide solution (224 c.c.) is heated for 7 hours at 90°, the acetyl group is completely removed. This is shown by the precipitation by acetic acid of *p*-aminophenylstibonic acid having without purification the composition $NH_2\cdot C_6H_4\cdot SbO_3H_2,4/3H_2O$, in agreement with that of the purified substance described by Schmidt (*Annalen*, 1922, **429**, 145). Under these conditions the alkaline solution, if kept for several days, deposits, together with a small amount of finely divided material poorer in carbon, which is removed by levigation, large crystals of sodium *p*-aminophenylstibonate, which when dried over sulphuric acid at room temperature consist of the dihydrate $NH_2\cdot C_6H_4\cdot SbO_3HNa,2H_2O$ (12·8 g.). This may be dissolved in cold water and recrystallised by the addition of an equal volume of acetone (yield, 6·3 g.). It forms large, almost colourless, rectangular plates, soluble in 14 parts of water at 20° (Found: C, 22·4; H, 3·7; N, 4·4; Sb, 37·7; Na, 7·2. Calc. for $C_6H_7O_3NSbNa,2H_2O$: C, 22·4; H, 3·4; N, 4·4; Sb, 37·8; Na, 7·1%). The water of crystallisation is not lost completely below 160°, and at this temperature the substance begins to darken.—THE WELLCOME CHEMICAL RESEARCH LABORATORIES, LONDON, and WELLCOME CHEMICAL WORKS, DARTFORD. [*Received, February 18th*, 1938.]

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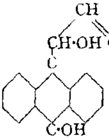
## 80. *Benzanthrones. Part I. The Mechanism of Bally's Reaction.*

By FAWZI G. BADDAR and FRANK LOUIS WARREN.

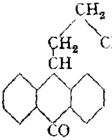
α-Ethylglycerol, which is converted into β-ethylacraldehyde by concentrated sulphuric acid, is condensed with anthranol under the conditions of Bally's reaction to give 1'-*ethyl*meso*benzanthrone*, the constitution of which is verified by ring closure of o-4'-*ethyl*-1'-*naphthylbenzoic acid*.

This establishes the validity of the mechanism advanced by Bally and Scholl for the formation of *meso*benzanthrone by the interaction of glycerol, anthranol, and concentrated sulphuric acid. Meerwein's mechanism would require the formation of 3'-ethyl*meso*benzanthrone.

*meso*Benzanthrone was first synthesised by Bally (*Ber.*, 1905, **38**, 194) by the action of glycerol and sulphuric acid on anthraquinone. Bally and Scholl (*Ber.*, 1911, **44**, 1656) maintained that the mechanism of the reaction was the reduction of anthraquinone to anthrone, which then condensed with acraldehyde, generated from the glycerol by the action of sulphuric acid, to yield the aldol condensation product (I). This then lost water to



(I.)



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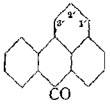

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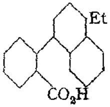

(IV.)

give the allylidene-anthrone, which cyclised to *meso*benzanthrone (III) with the loss of hydrogen, which was taken up in the reduction of more anthraquinone. This cyclisation is similar to that which acraldehyde-aniline undergoes on dry distillation (Koenigs, *Ber.*, 1880, **13**, 911); but there are difficulties in explaining this under the conditions of the experiment unless it is assumed that the cyclisation is due to the isomerisation of the unsaturated compound (I), as has been postulated by Darzens and his co-workers (*Compt. rend.*, 1926, **183**, 748, etc.) in the general synthesis of naphthalene derivatives.

Meerwein (*J. pr. Chem.*, 1918, **97**, 284) showed that anthrone can add benzylidene-malonic ester to give β-anthronyl-β-phenyl*iso*succinic ester; and he suggested that acraldehyde reacted additively with anthrone to produce β-anthronylpropaldehyde (II), which passed through 2′ : 3′-dihydro*meso*benzanthrone to *meso*benzanthrone—a cyclisation and dehydrogenation similar to that known to take place in the Skraup reaction (Blaise and Maire, *Bull. Soc. chim.*, 1908, **3**, 671).

The dehydration of α-ethylglycerol can occur in two ways to give either β-ethylacraldehyde or vinyl ethyl ketone. Catalytic dehydration gives the ketone and no aldehyde (Delaby, *Compt. rend.*, 1923, **117**, 690); but when α-ethylglycerol replaces glycerol in the Skraup reaction, a mixture of 2- and 4-ethylquinoline is produced, in which the former predominates and is even the essential constituent (Delaby and Hiron, *Compt. rend.*, 1930, **191**, 845). Since no practical details are given, we have repeated this experiment, following the conditions stated for 3-phenylquinoline (Warren, J., 1936, 1367), and have only been able to isolate 2-ethylquinoline. This fact shows directly the intermediate formation of β-ethylacraldehyde (Blaise and Maire, *loc. cit.*), the establishment of which gives a method of deciding between the two theories.

The condensation of α-ethylglycerol with anthranol in the presence of sulphuric acid results in the formation of a product which is identical with that derived from the ring closure of o-4′-*ethyl*-1′-*naphthylbenzoic acid* (IV) and therefore is 1′-*ethyl*meso*benzanthrone*, which is the product expected on the theory of Bally and Scholl (*loc. cit.*). Meerwein's mechanism (*loc. cit.*) would require the isolation of 3′-ethyl*meso*benzanthrone.

*Synthesis of* 1′-*Ethyl*meso*benzanthrone.*—1-Ethylnaphthalene was nitrated with fuming nitric acid at – 5° to give 4-*nitro*-1-*ethylnaphthalene*, which was reduced with stannous chloride to 4-ethyl-1-naphthylamine (compare Lesser and Glaser, *Annalen*, 1913, **402**, 11) which was transformed into 4-*iodo*-1-*ethylnaphthalene*. This was condensed with methy *o*-iodobenzoate by the Ullmann reaction (*Annalen*, 1904, **332**, 38) to give methyl *o*-4′ ethyl-1′-naphthylbenzoate. The temperature at which this condensation was effecte had a profound influence on the yield: at 280° with equimolecular proportions of th two iodo-compounds the yield was only 1% of the pure acid; but at 180° with one mol of the naphthalene and two moles of the ester the yield rose to 10% (compare Rule an Smith, J., 1937, 1096). Under the latter conditions iodobenzoic ester did not conden with 1-iodonaphthalene and the temperature had to be raised to 280° for the optimu yield. Ring closure of *o*-4′-ethyl-1′-naphthylbenzoic acid by the Friedel–Crafts reacti with the acid chloride gave 1′-ethyl*meso*benzanthrone and 2′-*ethyl*-3 : 4-*benzfluorenone*

the proportion of about 1 to 2 respectively, but cyclisation by warming the acid with concentrated sulphuric acid resulted mainly in the fluorenone. Similar results were obtained with *o*-1'-naphthylbenzoic acid, although Schaarschmidt and Georgeacopol (*Ber.*, 1918, **51**, 1086) report only the formation of *meso*benzanthrone by the Friedel–Crafts reaction.

## Experimental.

*Bally's Reaction with α-Ethylglycerol.*—Sulphuric acid (132 c.c.; 2·4 mols.) was stirred at room temperature while anthraquinone (9 g.; 0·043 mol.) was slowly added; when all had dissolved, water (5 c.c.) was added. The reactants were maintained at 38—42° while freshly precipitated copper (6 g.; 0·01 mol.) was added during 90 minutes; after 3 hours the copper had dissolved, the mixture acquired a yellow-brown colour, and some anthranol separated. A mixture of α-ethylglycerol (14·4 g.; 0·12 mol.) and water (14 c.c.) was added during 50 minutes while the temperature was raised to 80°; the whole was then maintained at 100° for 2½ hours. The progress of the reaction was shown by the development of a red colour; and considerable care was exercised in heating to avoid charring, which occurred only too readily. The whole was cooled and poured into boiling water (500 c.c.), boiled for a few minutes, and kept overnight. The precipitate was collected, washed with water, and boiled for 40 minutes with 1% sodium hydroxide solution (150 c.c.) to dissolve unchanged anthranol. The solution, which could not be filtered, was shaken several times with benzene, and the emulsion centrifuged into two layers. The combined benzene extracts were boiled for 2 hours with animal charcoal and filtered, and the solvent removed principally by distillation and finally by evaporation in a vacuum at the ordinary temperature. The crystals that separated were pressed on a porous plate to remove oily material and recrystallised from methyl alcohol, from which *1'-ethyl*meso*benzanthrone* separated in yellow needles (0·5 g.), m. p. 106°, showing no depression when mixed with the specimen obtained by ring closure as below (Found: C, 88·3; H, 5·5. $C_{19}H_{14}O$ requires C, 88·3; H, 5·5%).

*4-Nitro-1-ethylnaphthalene.*—To 1-ethylnaphthalene (95 g.; 1 mol.) in glacial acetic acid (137 c.c.) at − 5°, 99% nitric acid (51 g.; 1·3 mols.) was added very slowly with stirring. The mixture was kept at 0° for 4 days, ice added, the precipitated oil extracted with benzene, and the extract washed with water and sodium carbonate solution. The product which distilled at 160—170°/3 mm. was redistilled. *4-Nitro-1-ethylnaphthalene* was obtained as a yellow mobile liquid, b. p. 164—165°/3 mm., $d_{4^\circ}^{25^\circ}$ 1·190. Yield 60 g., *i.e.*, 49% of the theoretical (Found: C, 72·0; H, 5·4; N, 6·7. $C_{12}H_{11}O_2N$ requires C, 71·6; H, 5·5; N, 7·0%).

*4-Ethyl-1-naphthylamine.*—A well-stirred solution of stannous chloride (187 g.; 3·1 mols.) in concentrated hydrochloric acid (80 g.; 3·3 mols.) was heated on a water-bath and 4-nitro-1-ethylnaphthalene (30 g.; 0·5 mol.), dissolved in hot alcohol (30 c.c.), was added during 1 hour. Pure nitro-compound (30 g.) was then added more rapidly, and heating continued for another hour. The whole was steam-distilled to remove unreduced nitro-compounds, made alkaline, steam passed to effect the separation of the base from the solid, and the solution extracted with ether. 4-Ethyl-1-naphthylamine was isolated as a dark-coloured oil, readily oxidised in the air, b. p. 170°/8 mm. Yield 35 g., *i.e.*, 69% of the theoretical. *4-Ethylaceto-1-naphthalide* separated from methyl alcohol in colourless needles, m. p. 151° (Found: C, 78·6; H, 7·1; N, 6·7. $C_{14}H_{15}ON$ requires C, 78·8; H, 7·1; N, 6·6%).

*4-Iodo-1-ethylnaphthalene.*—The amine (38 g.; 1 mol.), dissolved in hot 2N-sulphuric acid (440 c.c.; 2 mols.), was cooled quickly to 0° and diazotised with sodium nitrite (14·3 g.; 0·93 mol.) in water (30 c.c.). Potassium iodide (44 g.; 1·2 mols.), dissolved in water, was added at 0° and the solution was stirred for 2 hours, heated to 100°, cooled, and treated with sodium bisulphite. The separated oil, extracted with benzene, was distilled to give *4-iodo-1-ethylnaphthalene* as a light yellow oil, b. p. 170°/7 mm., readily decomposed on heating at the ordinary pressure, especially in the presence of moisture. Yield 30 g., *i.e.*, 48% of the theoretical (Found: I, 45·4. $C_{12}H_{11}I$ requires I, 45·0%).

*o-4'-Ethyl-1'-naphthylbenzoic Acid.*—A mixture of 4-iodo-1-ethylnaphthalene (5 g.; 1 mol.) and methyl *o*-iodobenzoate (10 g.; 2·1 mols.) in a dry tube fitted with a mercury-sealed stirrer was heated to 180°, copper-bronze added during 45 minutes, and heating continued for 4 hours. The oil was extracted with acetone and hydrolysed with alcoholic potassium hydroxide, the alcohol evaporated, and the product taken up in water. After extraction with benzene to remove neutral compounds and boiling with animal charcoal, the solution was acidified and extracted with ether. The sticky solid from the ethereal extract was lixiviated with benzene and filtered from diphenic acid. The benzene extract gave an oil, which was esterified and distilled. The

distillate, b. p. about 200°/1 mm., gave on hydrolysis *o-4'-ethyl-1'-naphthylbenzoic acid,* which crystallised from methyl alcohol in long colourless cubes, m. p. 176°. Yield 0·5 g., equivalent to 10% of the theoretical calculated on the iodoethylnaphthalene (Found: C, 82·5; H, 5·7. $C_{19}H_{16}O_2$ requires C, 82·6; H, 5·8%).

*1'-Ethyl*meso*benzanthrone.*—(a) *Friedel–Crafts reaction* (compare Schaarschmidt and Georgeacopol, *loc. cit.*). The above acid (0·15 g.) gave a neutral product (0·13 g.), which crystallised from methyl alcohol to give a mixture of yellow and orange-red crystals; these were separated mechanically. The yellow material, recrystallised from methyl alcohol, gave 1'-ethyl*meso*benzanthrone in yellow needles (0·03 g.), m. p. 106°, slightly soluble in alcohol with an orange-green fluorescence, and giving a deep red colour with concentrated sulphuric acid (Found: C, 88·2; H, 5·4. Calc. for $C_{19}H_{14}O$: C, 88·3; H, 5·5%). The orange-red crystals were recrystallised from acetic acid to give *2'-ethyl-3 : 4-benzfluorenone* (0·06 g.), m. p. 139°, which gave a green colour with concentrated sulphuric acid (Found: C, 87·9; H, 5·5. $C_{19}H_{14}O$ requires C, 88·3; H, 5·5%).

(b) The above acid (0·15 g.) was heated with 90% sulphuric acid (10 c.c.) at 50° for 2 hours, and the solid precipitated with water was warmed with sodium carbonate solution, washed, and fractionally crystallised as above. The yield was 0·005 g. of 1'-ethyl*meso*benzanthrone and 0·1 g. of 2'-ethyl-3 : 4-benzfluorenone.

*o-1'-Naphthylbenzoic Acid.*—1-Iodonaphthalene (5 g.; 1 mol.) and methyl *o*-iodobenzoate (10 g.; 1·94 mols.) were condensed in the presence of copper-bronze (15 g.; 12 mols.) at 280° as above. The benzene solution, filtered from the diphenic acid, gave a semi-solid, which on crystallisation from methyl alcohol gave *o*-1'-naphthylbenzoic acid, m. p. 161° (Schaarschmidt and Georgeacopol, *loc. cit.*, give 161°), the yield being 30% of the theoretical calculated on the iodonaphthalene. Ring-closure of the acid by the two methods described above gave a mixture of *meso*benzanthrone and benzfluorenone in corresponding yields.

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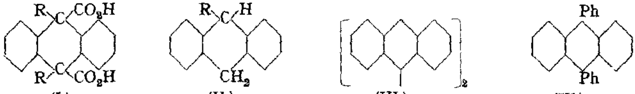
## 81. *The Configuration of Heterocyclic Compounds. Part VIII. The Configuration of Anthracene, 9 : 10-Dihydroanthracene, Phenazine, 9 : 10-Dimethyl-9 : 10-dihydrophenazine, Thianthren, and Selenanthren.*

By ISHBEL G. M. CAMPBELL, CATHERINE G. LE FÈVRE, R. J. W. LE FÈVRE, and E. E. TURNER.

Theoretical considerations show that a molecule of the general formula (VI) will be least strained when it is folded, provided that the atom or group X prefers a valency angle approximating to the tetrahedral angle. For example, 9 : 10-dihydroanthracene (VI; X = $CH_2$) should be folded, and evidence is given below that the dipole moment of the hydrocarbon is not zero, but is of the same order as that of dibenzyl. The less easily interpreted moment of 9 : 10-dimethyl-9 : 10-dihydrophenazine (VI; X = NMe) could correspond with folding of the molecule about the X—X axis and a certain disposition of the N—Me bonds.

A paper by Schlenk and Bergmann, describing novel stereoisomerism among anthracene derivatives, is discussed.

IN 1928, Schlenk and Bergmann (*Annalen*, **463**, 1) stated that in preparing various derivatives of anthracene and dihydroanthracene they had obtained more forms than seemed then to be required by stereochemical theory. They described (*a*) three forms each of

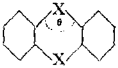



(I.) (II.) (III.) (IV.)

9 : 10-dihydroanthracene-9 : 10-dicarboxylic acid (I; R = H) and of its 9 : 10-diphenyl derivative (I; R = Ph), (*b*) two forms each of 9-phenyl-9 : 10-dihydroanthracene (II;

R = Ph) and 9 : 10-dihydroanthracene-9-carboxylic acid (II; R = $CO_2H$), (*c*) two forms of 9 : 9′-dianthranyl (III) and two forms of 9 : 10-diphenylanthracene (IV). They explained the third form of each of the compounds (I) and the second form of each of the compounds (II), (III), and (IV) as being due to double folding of the molecule *at the two fused bonds*, as indicated in (V).

(V.)

 (VI.)

Meerwein and Migge (*Ber.*, 1929, **62**, 1046) showed that Schlenk and Bergmann's second 9 : 10-dihydroanthracene-9-carboxylic acid was probably a mixture and not a second form at all, but did not comment on the general feasibility of the Schlenk–Bergmann space formulæ, although from a footnote in their paper it is clear that they were prepared to *discuss* the possibility that anthracene was not necessarily planar. It may be noted that the Schlenk–Bergmann isomerides were not referred to in Freudenberg's "Stereochemie," 1933.

In 1932, Bergmann and Tschudnowsky (*Ber.*, **65**, 458), finding thianthren (VI; X = S) to possess a considerable dipole moment, suggested, without reference to the disposition of the aromatic nuclei with respect to the centre ring, that the latter was "gewinkelt" about the line joining the sulphur atoms, and this has been interpreted by Bennett and Glasstone (J., 1934, 128) as implying that Bergmann and Tschudnowsky thought, with themselves, that the molecule *as a whole* was folded about the S—S axis. It is at any rate clear that Bergmann and Tschudnowsky did not associate the question of the configuration of thianthren with that of related carbon compounds (VI; X = saturated carbon), and in particular did not associate it with the configuration of their 1928 isomerides (I—IV). Bennett and Glasstone were actually the first to make clear the nature of the folding of thianthren, and their work led Lesslie and Turner (J., 1934, 1170; 1935, 1268; 1936, 730) to attempt, and accomplish, the optical resolution of three different 10-substituted phenoxarsine-2-carboxylic acids, the grounds for this attempt being that the phenoxarsine molecule might be folded with greater rigidity than the thianthren molecule (see below).

The general problem concerning the configuration of compounds of type (VI) has, however, never been stated, and it is with this that we are now concerned.

The centres of the carbon atoms in the aromatic nucleus form a regular hexagon. Save for particular reasons in special cases, the extra-annular valency direction of each nuclear carbon atom passes, if produced backwards, through the centre of the hexagon. Formula (V) does not comply with this requirement and is therefore not admissible.

For a compound of the general formula (VI), in which two aromatic nuclei are joined by *single* bonds through two atoms, X, of the same element, whatever the nature of X, two corollaries follow: (1) If the molecule is planar, the angle, $\theta$, at X is 120°. (2) If $\theta$ is 109·5°, the tetrahedral angle, the molecule will be folded about the axis X—X, so that the angle of fold ($\psi$) between the two planes each containing one aromatic nucleus and both atoms X, is approximately 141°. The flexibility of the molecule about the X—X axis will naturally vary from one substance to another.

A compound of type (VI) will therefore be planar when the preferred valency angle of X is equal to or greater than 120°, as has been pointed out by Bennett, Earp, and Glasstone (J., 1934, 1179) for the case of diphenylene dioxide (VI; X = O). More interesting are the numerous examples of compounds of type (VI) in which X is an element which prefers a valency angle less than 120°, *e.g.*, sulphur (as shown by the configuration of thianthren) or *carbon*. It is at once clear that 9 : 10-dihydroanthracene (VI; X = $CH_2$) will only be strainless when it is folded about the $CH_2$—$CH_2$ axis, and this folding should cause the molecule to possess a measurable dipole moment.

We have determined the dipole moment of 9 : 10-dihydroanthracene, and for comparative purposes that of anthracene. We also give details of the experimental work on selenanthren (VI; X = Se) referred to in Part VI (Thompson and Turner, this vol., p. 29). Thianthren has been used as a standard for comparison.

Little information is available as to the preferred nitrogen valency angle, although ammonia itself values from 94° to 116° have been given (Badger and Mecke, *Z. physikal. em.*, 1929, *B*, **5**, 333; Barker, *Physical Rev.*, 1928, **31**, 1131; 1929, **33**, 684; Lueg and edfeld, *Z. Physik*, 1932, **75**, 599). It seems probable that 9 : 10-dimethyl-9 : 10-dihydro-enazine (VI; X = NMe) would be folded. The results of examining this phenazine erivative are stated and discussed below.

*Dipole-moment Measurements.*—The requisite observed data are in Table I under the llowing headings: $w_1$, the weight fraction of the solute in the solutions; $\varepsilon_{25°}^{1200}$, the ielectric constants of the solutions measured at approximately 1200 kc. and 25°; $d_{4°}^{25°}$; nd finally, $n_D^{25°}$. From these are derived $\alpha\varepsilon_2$ and $\beta d_2$, constants containing the coefficients f change of dielectric constant and density with solute concentration ($w_1$). Observational rregularities can most easily be discerned in these columns, which also show that the inear relationships relating $\varepsilon_{12}$ and $w_1$, and $d_{12}$ and $w_1$, hold in the present cases. The total polarisations at infinite dilution are calculated (Table II) from the mean values of $\alpha\varepsilon_2$ and $\beta$, etc., by the formula $(P_1)_\infty = M[p_2(1-\beta) + C\alpha\varepsilon_2]$ (compare Le Fèvre and Vine, J., 1937, 1805), in which $M$ is the molecular weight of the solute, and $p$ and $C$ are, for the sample of benzene used in the present work, 0·34086 c.c. and 0·18809, respectively.

The molecular refractions are derived from the appropriate measurements by the mixture rule $[R_L]_D = M_1[r_2 + (r_{12} - r_2)/w_1]$, in which $r_2$ and $r_{12}$ are the specific refractions of the solvent and solution; $r_2 = 0·33503$ for the benzene used.

TABLE I.

| $100\,w_1$. | $\varepsilon_{25°}^{1200}$. | $d_{4°}^{25°}$. | $\alpha\varepsilon_2$. | $\beta d_2$. | $n_D^{25°}$. | $[R_L]_D$. |
|---|---|---|---|---|---|---|
| 0 | 2·2725 | 0·87378 | — | — | 1·49724 | — |
| | | | Anthracene. | | | |
| 0·1623 | 2·2735 | 0·87410 | 0·616 | 0·197 | — | — |
| 0·4821 | 2·2756 | 0·87471 | 0·643 | 0·194 | 1·49820 | 66·7 |
| 0·6003 | 2·2762 | 0·87494 | 0·616 | 0·193 | — | — |
| 0·6015 | 2·2762 | 0·87495 | 0·615 | 0·195 | 1·49866 | 67·4 |
| | | | 9 : 10-Dihydroanthracene. | | | |
| 0·89325 | 2·2765 | 0·87532 | 0·445 | 0·173 | — | — |
| 0·8942 | 2·2765 | 0·87533 | 0·447 | 0·174 | 1·49813 | 58·5 |
| 0·8981 | 2·2765 | 0·87535 | 0·445 | 0·173 | 1·49820 | 59·5 |
| 0·9493 | 2·2767 | 0·87541 | 0·442 | 0·172 | 1·49828 | 59·7 |
| | | | Phenazine. | | | |
| 0·5503 | 2·2757 | 0·87517 | 0·581 | 0·253 | 1·49828 | 62·3 |
| 0·66045 | 2·2762 | 0·87544 | 0·560 | 0·251 | 1·49850 | 62·5 |
| 0·6715 | 2·2763 | 0·87546 | 0·571 | 0·251 | — | — |
| 0·6856 | 2·2764 | 0·87551 | 0·569 | 0·253 | — | — |
| | | | 9 : 10-Dimethyl-9 : 10-dihydrophenazine. | | | |
| 0·1475 | 2·2734 | 0·87412 | 0·610 | 0·230 | — | — |
| 0·1924 | 2·2736 | 0·87422 | 0·590 | 0·228 | — | — |
| 0·4649 | 2·2752 | 0·87485 | 0·580 | 0·230 | — | — |
| 0·8928 | 2·2778 | 0·87585 | 0·594 | 0·232 | 1·49873 | 71·5 |
| 1·0673 | 2·2788 | 0·87623 | 0·590 | 0·230 | 1·49894 | 70·9 |
| | | | Thianthren. | | | |
| 0·2474 | 2·2766 | 0·87450 | 1·657 | 0·291 | 1·49761 | 66·3 |
| 0·3279 | 2·2780 | 0·87476 | 1·677 | 0·299 | 1·49773 | 65·8 |
| 0·4385 | 2·2800 | 0·87507 | 1·710 | 0·294 | 1·49788 | 66·0 |
| 0·4801 | 2·2806 | 0·87524 | 1·687 | 0·304 | 1·49795 | 65·2 |
| | | | Selenanthren. | | | |
| 0·2906 | 2·2756 | 0·87509 | 1·067 | 0·451 | 1·49761 | (73·0) |
| 0·4821 | 2·2776 | 0·87596 | 1·058 | 0·452 | 1·49781 | 71·2 |
| 0·5211 | 2·2780 | 0·87616 | 1·055 | 0·457 | 1·49790 | 71·8 |
| 0·5613 | 2·2784 | 0·87632 | 1·051 | 0·453 | 1·49793 | 71·9 |

TABLE II.

| Substance. | *M*. | Mean values of $\alpha\epsilon_2$. | $\beta$. | $(P)_\infty$. | $[R_L]_D$. | $\mu$. |
|---|---|---|---|---|---|---|
| Anthracene | 178 | 0·622 | 0·223 | 67·9 | 67 | *ca.* 0 |
| Dihydroanthracene | 180 | 0·445 | 0·198 | 64·3 | 60 | *ca.* 0·4 |
| Phenazine | 180 | 0·570 | 0·288 | 63·0 | 63 | *ca.* 0 |
| Dimethyldihydrophenazine | 210 | 0·593 | 0·263 | 76·2 | 72 | *ca.* 0·4 |
| Thianthren | 216 | 1·683 | 0·340 | 117·0 | 66 | 1·57 |
| Selenanthren | 310·5 | 1·058 | 0·518 | 112·8 | 72 | 1·41 |

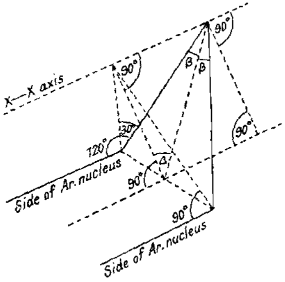
*Remarks.*—Measurements previously recorded for phenazine and thianthren are:

| | Thianthren. | | | | | Phenazine. |
|---|---|---|---|---|---|---|
| Temp. | 21·8°. | 25°. | 50°. | 24·92°. | 24°. | 14·9°. |
| Solvent | $C_6H_6$ | $C_6H_6$ | $C_6H_6$ | $CCl_4$ | $CS_2$ | $C_6H_6$ |
| Moment | 1·7 [1] | 1·41 [2] | 1·41 [2] | 1·54 [3] | 1·47 [2] | 0 [4] |

[1] Bergmann and Tschudnowsky, *loc. cit.* [2] Smyth and Walls, *J. Chem. Physics*, 1933, **1**, 337.
[3] Bennett and Glasstone, *loc. cit.* [4] Bergmann, Engel, and Meyer, *Ber.*, 1932, **65**, 446.

Our result for thianthren is in good agreement with that of Bennett and Glasstone. In both cases the orientation polarisation is the same, *viz.*, 51 c.c., from which, without further correction, the moment is calculable as 1·57 D. For phenazine, Bergmann, Engel, and Meyer reported a molecular refractivity in excess over the total polarisation by more than 10 c.c. Our figures have a greater *prima facie* probability and indicate a zero moment for the substance.

The moments of dihydroanthracene and dimethyldihydrophenazine are too small to evaluate accurately. This arises because their calculation involves square roots, which, being small differences between two relatively large numbers, are liable to contain the accumulated errors of both. These uncertainties are not only experimental in origin, but are inherent in the method, which accepts the molecular refraction as the sum of the electronic and the atomic polarisation.

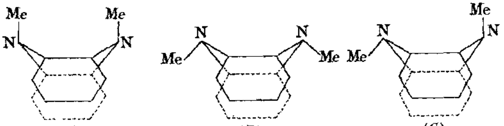



On the other hand, the fact that anthracene and phenazine, with flat molecules, show total polarisations which are practically equal to the corresponding refractions (so that $\mu = 0$) strengthens the likelihood that the two dihydro-derivatives have finite moments greater than zero.

The present results therefore support the conclusion that certain molecules of type (VI) exist largely in non-planar configurations, stabilised by the adoption by the atom or group X of preferred valency angles ($\theta = 2\beta$) of about 110°. The simple construction given in the figure shows that if $\theta = 2\beta = 110°$ and the extra-nuclear valency angles are 120°, $\sin \Delta = 1/(2 \cos \beta)$, whence $\Delta = 61°$, *i.e.*, the resultant moments of these compounds should arise from two vectors compounded at 122°. Approximate values for each of the latter would be the moment of the corresponding substance: $Ph_2S$, $Ph_2Se$, $Ph_2CH_2$ and $Ph_2NMe$. The last is not yet available, but for the first three, $\mu \doteqdot 1·5$, 1·4, and 0·4 D., respectively. The moments of thianthren, selenanthren, and dihydroanthracene calculated from these figures are 1·45, 1·36, and 0·39, respectively, in close agreement with the present experimental results.

*The Small Moment of Dimethyldihydrophenazine.*—Three probable configurations for this substance, involving three different dispositions of the N—Me bonds, are shown in exaggerated perspective. In type *A* the Me→N links would subtend an angle of about 120° with the planes containing the two associated pairs of Ar→N links. This is a highly

probable arrangement and would give a molecular model in which the Me→N link moments together would oppose in *nearly antiparallel alinement* the resultant moment




(*A*.) (*B*.) (*C*.)

arising from the four Ar→N vectors. Such a structure might well have only a small molecular resultant moment, so that the value now found for dimethyldihydrophenazine does not necessarily disprove occurrence of folding in the molecule. Moreover, it seems unlikely that the dipole moment observed owes its origin merely to a *cis*-disposition of N—Me valencies in a non-folded structure: the only examples of *cis-trans*-isomerism among such derivatives of tervalent nitrogen are the "quinoline dicyanides" of Mumm and Ludwig (*Annalen*, 1934, **514**, 34).

In view of the failure of attempts (Bennett, Lesslie, and Turner, J., 1937, 444; Keats, *ibid.*, p. 1592) to resolve substituted thianthrens, it seems unlikely that nuclear substituted dihydroanthracenes would (usually) be configurationally stable enough to be resolvable. At the same time, although a configuration such as (V) for anthracene is inadmissible, for reasons stated above, yet a molecule of type (I), if *stably* folded about the 9 : 10-axis, should exist in three forms, and one of type (II) in two forms, corresponding with the experimental evidence of Schlenk and Bergmann. On the other hand, anthracene, a compound not belonging to type (VI), is beyond doubt planar (Robertson, *Proc. Roy. Soc.*, 1933, **140**, 79), and for (III) and (IV) only one form in each case is conceivable, contrary to the experimental evidence of Schlenk and Bergmann.

A possibility which has always received our consideration becomes a probability as a result of the present study of dimethyldihydrophenazine, and this is that in a phenoxarsine the folding of the molecule and the natural disposition of the valencies of the arsenic atom tend to a mutual stabilisation of configuration.

## Experimental.

*Preparation of Phenazine.*—This was found to be less readily effected than would be gathered from the literature. Ris's method (*Ber.*, 1886, **19**, 2206) of heating catechol with *o*-phenylenediamine under pressure was extremely unsatisfactory. The condensation of *o*-nitrodiphenylamine with *o*-aminodiphenylamine in presence of sodium acetate (Kehrmann and Havas, *Ber.*, 1913, **46**, 341) gave a very poor yield. The method of Wohl and Aue (*Ber.*, 1901, **34**, 2246), in which aniline is heated with nitrobenzene in presence of alkali, was tedious and gave poor yields of phenazine. We found, however, that distillation of *o*-aminodiphenylamine with litharge (Fischer and Heiler, *Ber.*, 1893, **26**, 383) provided a convenient method (contrast McCombie, J., 1928, 353). The details of our synthesis are as follows:

*o*-Nitrodiphenylamine was prepared by a modification of the method of Kehrmann and Havas (*loc. cit.*): we noted that when a mixture of 100 g. of *o*-chloronitrobenzene, 140 g. of aniline, and 52 g. of fused sodium acetate was heated under reflux in a bath kept at 225—230°, the reaction mixture remained at a temperature of about 183° for the first 6 hours and finally rose to about 200° during the next 9 hours. Following the instructions of Kehrmann and Havas, we obtained poor yields, but operating as described above our yield of pure *o*-nitrodiphenylamine was 88 g.

The nitro-compound (150 g.) was reduced at boiling water-bath temperature with one part of iron filings in presence of water and a little acetic acid. Extraction of the reaction mixture with alcohol, followed by filtration and addition of water, gave the base, which, after being crystallised from alcohol, was pure (110 g.).

The conversion of aminodiphenylamine into phenazine was effected by heating an intimate mixture of 20 g. of the base with 200 g. of litharge in a wide combustion tube until no more material distilled. The crude distillate was crushed, mixed with 2 parts of litharge, and slowly

sublimed through a layer of litharge in an evaporating basin covered with a clock-glass. After being crystallised from alcohol, the phenazine was pure (8 g.).

*Phenazine methosulphate.* The procedure of Kehrmann and Havas (*loc. cit.*) was modified: 10 g. of pure methyl sulphate were added to a solution of 10 g. of phenazine in 50 c.c. of dried nitrobenzene at 120°. The mixture was kept at 100—110° for 10 minutes, by which time the methosulphate began to crystallise. Pure ether was added to the cooled mixture. The solid was collected, washed with ether, and crystallised from the least absolute alcohol (yield, 10—11 g.).

9 : 10-Dimethyl-9 : 10-dihydrophenazine was obtained by the method outlined by McIlwain (J., 1937, 1711), but since we had considerable difficulty with the preparation we give the actual conditions used. A Grignard reagent, prepared from 1·2 g. of magnesium and 3·2 c.c. of methyl iodide in 80 c.c. of ether, was slowly added to a suspension of 8 g. of finely ground phenazine methosulphate in 400 c.c. of ether. A vigorous current of dry nitrogen was passed through the mixture, which was well cooled. After addition of the reagent, the whole was boiled under reflux for 2 hours and then allowed to cool in a slow current of nitrogen. Ice and water were added. The ethereal layer was separated, and washed with water and dilute sodium bisulphite solution [washing with 5% sulphuric acid (McIlwain) diminished the yield]. The ether was removed, and the residue crystallised 3 times from absolute alcohol. The dimethyl base (1 g.) formed prisms, m. p. 152—153°. McIlwain's yields were never attained, in spite of the fact that we found that the dimethyl base was extracted to some extent from an ethereal solution by 5% sulphuric acid.

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## 82. *Methylene.*

By T. G. PEARSON, R. H. PURCELL, and G. S. SAIGH.

For many years the methylene radical has been of theoretical importance owing to its postulated existence as an intermediate in the combustion and decomposition of various organic molecules. Previous attempts to show the presence of the radical directly have either failed or led to contradictory conclusions.

In the present paper an account is given of its isolation from both keten and diazomethane by thermal and photochemical methods. Its properties have been studied—it behaves as a very reactive molecule rather than a free radical—and the results obtained enable the discrepancies in the literature to be reconciled.

THE first attempt to establish the existence of a stable bivalent form of carbon was described by Nef in a series of papers (*Annalen*, 1892, **270**, 267; 1894, **280**, 291; 1895, **287**, 265; 1897, **298**, 202) covering over 385 pages and describing the properties and reactions of more than 100 compounds. He concluded "that organic compounds readily undergo a primary decomposition into a stable smaller molecule and a radical containing bivalent carbon." To-day it is recognised that, although many of his premises transgress accepted views of valency and energetics, some of his conclusions are close to the truth, for example: "The exclusive production of formaldehyde when ethylene is burnt in oxygen at 400° is . . . explained on the assumption that the hydrocarbon is dissociated into methylene" (*Abstracts*, 1898, **74**, 102).

Much earlier, Marchand (*J. pr. Chem.*, 1839, **36**, 478) had obtained large quantities of methane during the decomposition of ethylene at bright red heat, and concluded that the ultimate resolution of a hydrocarbon into its elements at high temperatures cannot be regarded as the result of a single chemical change. These views were clarified by Bone and Coward (J., 1908, **93**, 1191) in an investigation of the decomposition of methane, ethane, ethylene, and acetylene between 500° and 1200°. An examination of the residues revealed the existence of intermediate stages, and the authors supposed that the primary effect, in the cases of ethane and ethylene, causes an elimination of hydrogen and the dissolution of the bond between the carbon atoms to yield residues such as $:CH_2$ and $\vdots CH$. This

research was the first of a long series of investigations by Bone and his collaborators, in consequence of which he (*Trans. Faraday Soc.*, 1934, **30**, 150) reaffirmed his belief in the existence of the methylene radical.

In 1932 Kassel (*J. Amer. Chem. Soc.*, 1932, **54**, 3949) studied the decomposition of methane at 700—800°, and showed that the reaction is homogeneous and kinetically of the first order. Of the two ways in which the reaction might conceivably occur, *viz.*,

$$CH_4 = CH_3 + H - 125 \text{ kg.-cals.}$$
$$CH_4 = CH_2 + H_2 - 47 \text{ kg.-cals.}$$

he favoured the latter on the ground of a comparison of the heats of these reactions and the experimental heat of activation, and concluded that methylene is a comparatively inert substance, the energies of activation for its addition reactions with methane, hydrogen, and itself being 44, 32, and 24 kg.-cals. respectively.

Meanwhile, Schmidlin and Bergmann (*Ber.*, 1910, **43**, 2821) discovered that above 600° acetone yields not only keten but also ethylene in increasing amounts, and its presence was ascribed to the methylene radicals from keten.

The first positive evidence was adduced from photochemical experiments. Lardy (*J. Chim. physique*, 1924, **21**, 353) recorded the absorption spectrum of keten, noted its resemblance to that of acetone, and observed a series of five diffuse bands in the region corresponding to the carbonyl group, the significance of which was subsequently revealed by Norrish, Crone, and Saltmarsh (J., 1933, 1533). They measured the wave-lengths of the various bands, established that the region most responsible for the photochemical change corresponded with the absorption region of the carbonyl group, and found that the dissociation was accompanied by the formation of ethylene and carbon monoxide in the ratio of 1 : 2. These results led the authors to conclude that: (1) " The primary change is simply interpreted as a splitting of the molecule at the olefinic bond according to the equation $CH_2{:}CO + h\nu = CH_2 + CO$, the liberated $CH_2$ reacting further with undecomposed keten, to give ethylene and carbon monoxide: $CH_2{:}CO + CH_2 = C_2H_4 + CO$."

(2) " The energy relationships from the primary change when analysed, show that it cannot be represented purely as a rupture of the olefinic bond; they are, however, consistent with a decomposition into $CH_2$ and CO molecules, each containing carbon in the bivalent form." This deduction was made in order to reconcile the spectroscopic data with the known heats of formation, the minimum quantum effecting decomposition corresponding with $\lambda = 3850$ A., or 74 kg.-cals. per mol., the maximum with 2600 A. or 110 kg.-cals. per mol., neither of which is comparable with the 167 kg.-cals. necessary for the rupture of the olefinic bond in the ordinary way to yield CO and $CH_2$ *radicals*.

Ross and Kistiakowsky (*J. Amer. Chem. Soc.*, 1934, **56**, 112) repeated and confirmed these experiments and determined in addition the overall quantum yield of the reaction. They obtained the values 1·17, 1·03, 1·11, 1·19, 0·97, and 0·98 (mean 1·08) at 3130 A., smaller values at 3600 A., whilst at longer wave-lengths the photo-reactions became negligible. Since in the region of maximum absorption the quantum yield was close to unity, they were unable to agree with Norrish's secondary reaction, $CH_2{:}CO + CH_2 = CO + C_2H_4$, and concluded that the ethylene is produced by direct union of methylene radicals. Subsequently, Norrish and his collaborators (*ibid.*, p. 1644) attempted to justify their secondary mechanism by pointing out that the quantum yield of a primary reaction for a polyatomic molecule may be less than unity over a considerable range of frequencies, since a large part of the absorbed energy may be dissipated as heat (Auger effect) in the chromophoric carbonyl group. In this case, the quantum yield should increase towards a maximum as the magnitude of the absorbed quantum exceeds by greater amounts the energy necessary for the fission of the molecules. This would lead to an overall yield of 2 if the mechanism of Norrish and his colleagues is correct, and 1 for that proposed by Ross and Kistiakowsky. The fact that the values were less than unity at 3650 A., and somewhat exceeded it at 3130 A. was held to lend probability to the theory of the former school.

Numerous unsuccessful attempts appear to have been made to establish by direct tests the presence of methylene in the decomposition of keten. F. O. Rice and his co-

workers (*ibid.*, p. 1760) made an extensive survey of the mode of preparation and properties of keten, but did not comment upon its thermal or photochemical decomposition, apart from a statement in their book ("The Aliphatic Free Radicals," Baltimore, 1935, p. 41) that keten is too stable to be used as a source of free radicals. Ross and Kistiakowsky (*loc. cit.*) mentioned that they intended to pursue the investigation of methylene, but have not reported any experimental results. Paneth and Lautsch (J., 1935, 380) effected the thermal dissociation of keten by passing a rapid stream of the gas through a heated quartz tube, but they were "unable to raise the temperature sufficiently to effect any appreciable decomposition, with the formation of free methylene," although keten is said to decompose at relatively low temperatures with the separation of carbon (Williamson, *J. Amer. Chem. Soc.*, 1934, **56**, 2212).

We have found that keten is not easily decomposed thermally to yield free radicals, but at the temperature attained by a quartz tube heated in a good blast Bunsen burner large quantities of free methyl are liberated, and have been detected and identified by their reactions with tellurium, antimony, and lead, but detectable concentrations of methylene were never obtained. When, however, keten was exposed to light in the region of 2580—3130 A., plenty of methylene was obtained and identified by the formation of the various polymers of telluro- and seleno-formaldehydes, $(TeCH_2)_x$ and $(SeCH_2)_x$, and their addition compounds with mercuric halides. There was no diminution in the concentration of the radicals while they passed along 80 cm. of 11-mm. diameter quartz tube during 0·05 sec., in which each radical must have made $3 \times 10^3$ impacts with the walls of the tube, and $4 \times 10^5$ impacts with other molecules. This surprising result, indicating as it does that methylene has an order of persistence entirely different from that of the alkyl radicals (half-value period, $5 \times 10^{-3}$ sec.), led us to examine the products of the thermal and photochemical dissociation of diazomethane, because Rice and Glasebrook (*J. Amer. Chem. Soc.*, 1934, **56**, 2381) had obtained methylene in its thermal decomposition, and, without recording data, had ascribed to it a life-period similar to that of methyl.

It has been known for some time that diazomethane vapour decomposes slowly at room temperature to yield nitrogen and a solid polymer of methylene melting at 128° (Bamberger and Tschirner, *Ber.*, 1900, **33**, 956). Steacie (*J. Physical Chem.*, 1931, **35**, 1493) established that the composition of the gaseous products at higher temperatures is approximately: $N_2$, 67; $C_2H_4$, 30; $CH_4$, etc., 2%, in satisfactory agreement with that calculated from the equation $2CH_2N_2 = 2N_2 + C_2H_4$. He found the reaction to be homogeneously bimolecular, independent of the presence of powdered quartz in the reaction vessel, and to have an activation energy of 36 kg.-cals. per mol. The results were held to be best explained by a mechanism involving, not free radicals, but excited molecules which reacted in direct collision, thus $CH_2N_2^* + CH_2N_2 \longrightarrow 2N_2 + C_2H_4$.

The mechanism of the photochemical decomposition was studied by Norrish and Kirkbride (J., 1933, 119). The absorption spectrum consists of a series of diffuse predissociation bands, stretching from about 4700 A. and merging into a continuum at about 4200 A. The reaction yields $N_2$, 91·3; $CH_4$, 4·2; $C_2H_4$, 13·1; $C_2H_6$, 9·4; $C_2H_8$, 3·0%, together with some condensable products (partly nitrogenous bases), is kinetically unimolecular, and has an overall quantum yield of 4—5 between 4360 and 3650 A. The authors argued that the primary photochemical process involves complete dissociation into methylene and nitrogen, $CH_2N_2 + h\nu \longrightarrow CH_2 + N_2$, followed by a short chain of secondary reactions consuming about four molecules of diazomethane.

The first direct evidence of the presence of methylene in the products of decomposition of diazomethane was obtained by Staudinger and Kupfer (*Ber.*, 1912, **45**, 501, 504, 508), who passed a mixture of diazomethane and carbon monoxide through a heated silica tube and identified keten amongst the effluent gases. Subsequent experimental results are very conflicting. Paneth and Lautsch (*loc. cit.*) studied many reactions in which methylene was likely to be liberated. Their experiments with keten have already been described. They next tried to prepare the radical from diazomethane by passing the gas rapidly through a quartz tube heated to 600°, using both helium and hydrogen as transport gases. For identification they chose benzoic acid and carbon: $C_6H_5{\cdot}CO_2H + CH_2 \longrightarrow C_6H_5{\cdot}CO_2CH_3$, $C + 2CH_2 \longrightarrow CH_2{:}C{:}CH_2$, but neither reagent was perceptibly affected. In another

experiment, to avoid the possibility of destroying the methylene in the hot tube, decomposition was effected by an electric discharge. Although the diazomethane was quantitatively decomposed, no methylene was detected. Finally, they sought to obtain the radical from the reaction $CH_2Cl_2 + 2Na \longrightarrow 2NaCl + CH_2$, the probable occurrence of which had been demonstrated by Hartel and Polanyi (*Z. physikal. Chem.*, 1930, *B*, **11**, 97). A wide variation in experimental conditions failed to reveal anything beyond a considerable deposition of carbon. They concluded that methylene is far inferior to methyl and ethyl in stability and required more refined methods for its isolation and identification. This conclusion was in agreement with some experiments which had been previously described by Belchetz (*Trans. Faraday Soc.*, 1934, **30**, 170). A rapid stream of methane at 0·01 mm. pressure was allowed to pass over a strongly heated platinum or carbon filament and then to impinge on a cooled surface, covered with tellurium or iodine. When the distance from the filament to the cooled surface exceeded the mean free path of the molecules, the methyl radical alone was identified. When the distance was within the mean free path, the tellurium mirror was attacked to yield a minute amount of a grey white solid ($TeCH_2$?) which reacted with bromine to yield a liquid of b. p. 103—108° (methylene bromide, b. p. 98·5°). The iodine mirror gave a heavy oil, b. p. 145° (methylene iodide, b. p. 180°). The discrepancy was ascribed to the presence of chloroform used in the extraction. The impure methylene iodide was therefore shaken for 15 minutes with mercury in the presence of chloroform, and the mixture filtered. The yield of fine yellow crystals remaining after evaporation of the chloroform had m. p. 230° ($CH_2I_2Hg$, m. p. 230°; Sakurai, J., 1881, **39**, 485). The existence of the methylene as a highly reactive molecule thus appeared to be conclusively established, although the brief statement of the results here recorded gives no idea of the difficulties encountered during the experimental manipulation. Belchetz's apparatus is ingenious and obviates the formation of secondary products, but the yields obtained are minute, so that unequivocal identification is almost impossible. Shortly after the publication of these experiments, Rice and Glasebrook (*loc. cit.*) obtained methylene by decomposing a rapid stream of diazomethane in a silica tube at temperatures below 500°. They obtained the following important results (cf., however, Rice, *Chem. Reviews*, 1935, **17**, 60): (1) Mirrors of tellurium, selenium, antimony, and arsenic were readily removed, whereas zinc, cadmium, thallium, lead, and bismuth were not attacked. (2) With tellurium, neither dimethyl telluride nor ditelluride was condensed in a trap immersed in liquid air, but a deep red solid was deposited in the walls of the tube just beyond the tellurium; this could just be sublimed at 100° in a high vacuum (even then with some decomposition), it was stable in air, insoluble in water and the usual organic solvents, decomposed at 110° to yield tellurium, and contained C, 8·28; H, 1·33 (Calc. for $CH_2Te$: C, 8·40; H, 1·41%). (3) Although they published no data, the authors stated that methylene has a life period similar to that of methyl and ethyl. (4) Heated above 700°, diazomethane gave only methyl radicals.

The properties of telluroformaldehyde observed by Rice and Glasebrook were so different from those described by Belchetz that Rice and Dooley (*J. Amer. Chem. Soc.*, 1934, **56**, 2747) were led to re-investigate the thermal decomposition of methane. Unfortunately, from the point of view of precise comparison, they used a quartz tube heated by an electric furnace. They were unable to detect any methylene, but obtained a large yield of methyl radicals, and doubted the validity of Belchetz's work. Later, Belchetz and Rideal (*ibid.*, 1935, **57**, 1168) repeated their former experiments, and although reaching the same conclusion concerning the primary formation of methylene, they were unable to reproduce any of their former results. Referring to telluroformaldehyde, they merely state that " the greyish substance which was considered formerly to be such a compound . . . must have consisted of a trace of hydrogen telluride and a little tellurium," whilst the m. p. of 230° obtained for the mercury–methylene iodide compound was ascribed to coincidence, since two compounds $Hg_2CH_2I_2$ and $HgCH_2I_2$ are formed simultaneously and their separation is extremely difficult. We have found it impossible to obtain a compound of fixed melting point merely by mixing methylene iodide and mercury, and in agreement with Sakurai (*loc. cit.*) observed that the compounds take, not 15 minutes, but days to form, are insoluble in chloroform, and can be separated by fractionation only in

methylene iodide. From the second paper, two facts emerge: methylene could be identified by conversion into formaldehyde, followed by the Schryver–Rimini test; and the existence was confirmed of the red solid polymeric telluroformaldehyde of Rice and Glasebrook, which was obtained in one experiment with tellurium mirrors. Furthermore, the necessity for collecting the methylene radical within the mean-free-path distance of its formation was established.

We have examined the photochemical and thermal dissociation of diazomethane streaming at a low pressure and high velocity through a silica tube. Free methylene has been identified in both processes by conversion into telluroformaldehyde. Its life period in the presence of excess of diazomethane but in the absence of a carrier gas was found to be $5\cdot0 \times 10^{-3}$ sec. when produced thermally, and $6\cdot4 \times 10^{-3}$ sec. when produced photochemically, values which are held to be identical within the limits imposed by unavoidable experimental differences. Methylene thus appears to have three different half-value periods: in methane it is of the order of the time taken to traverse the mean free path, say $10^{-7}$ sec., in diazomethane it is similar to that of an alkyl radical, $5 \times 10^{-3}$ sec., and in keten it is too long to be measured by the ordinary methods.

The experiments recorded in the later pages of this paper are concerned with the resolution of these paradoxes. It is demonstrated that free methylene is to be regarded rather as a highly reactive molecule than a free radical in the sense that methyl is. Its persistence is therefore entirely a function of its environment. We are thus forced to the conclusion that the carbon in methylene is essentially bivalent ($^3P$), as postulated by Nef, Kassel, Mecke (*Trans. Faraday Soc.*, 1934, **30**, 211), and Lennard-Jones (*ibid.*, p. 70), and especially emphasised by Norrish and his colleagues (see p. 410). These conclusions cover the whole of our experimental results, and serve to account for all the pertinent data recorded by other workers, which are discussed in detail later.

## Experimental.

*Preparation of Keten.*—After a careful examination of the methods available for the preparation of keten (Hurd, *J. Amer. Chem. Soc.*, 1923, **45**, 515, 3095; Ott, Schröter, and Packendorff, *J. pr. Chem.*, 1931, **130**, 170; Staudinger and Kubinsky, *Ber.*, 1909, **42**, 4213; Staudinger and Klever, *Ber.*, 1908, **41**, 594; Hurd and Tallyn, *J. Amer. Chem. Soc.*, 1925, **47**, 1427), we chose the pyrolysis of acetone on a vanadium pentoxide catalyst according to Berl and Kullmann (*Ber.*, 1932, **65**, 1114). After the system had been filled with nitrogen, acetone was vaporised in a flask immersed in boiling water, and carried through the furnace packed with pumice, which had been previously soaked in 5% ammonium vanadate solution and ignited. Excess of acetone was removed from the effluent gases in the water condenser, and in a glass spiral cooled to $-70°$, and the keten frozen out in a number of traps immersed in liquid air. At the completion of the run, the more volatile fractions were distilled slowly into one trap in a stream of nitrogen. The trap was sealed off, and immediately connected by a ground joint *A* to the purification train (Fig. 1), wherein the products were submitted to a rigorous fractional distillation.

After a prolonged investigation of the best experimental conditions (furnace at 700°, acetone vaporised at the rate of 20 c.c./min.), we obtained a yield of 3% of purified keten (calculated on the total acetone passing through the furnace). Higher yields under other conditions were invariably accompanied by larger amounts of impurity from which the keten could not be separated. Even under the best conditions, our final purified product held 3·8% of unsaturated hydrocarbons (bromine-water test) which we could not eliminate in spite of many attempts, for we were emulating Rice (*J. Amer. Chem. Soc.*, 1934, **56**, 1760, 2132, 2268) who had obtained 100% keten by the use of a vacuum fractionating column. The vapour pressures of a typical sample are recorded below, since no figures, except the b. p. $-41°$, are given in the literature.

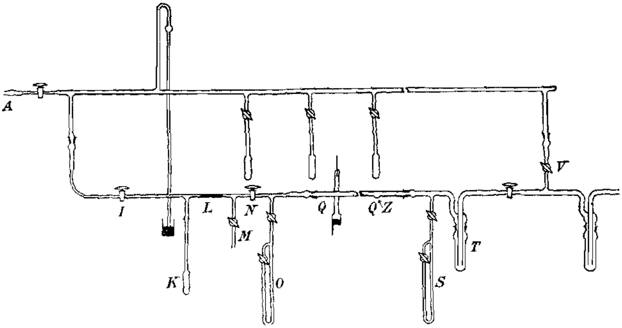
| Temp. ... | −71·0° | −72·0° | −75·5° | −90·0° | −91·0° | −92·0° | −93·0° | −94·0° | −94·5° | −120° |
|---|---|---|---|---|---|---|---|---|---|---|
| Press., cm. Hg ...... | 14·8 | 14·6 | 13·1 | 3·1 | 3·1 | 2·7 | 2·5 | 2·5 | 2·3 | 0·4 |

This keten was used in our experiments, since we did not anticipate difficulties from the presence of the unsaturated hydrocarbons.

The apparatus used in studying the products of dissociation is shown in Fig. 1. The purification train between *I* and *V* in the upper part of the diagram formed a part of the system to enable the keten to be redistilled during a series of experiments without being exposed to the air.

The purified keten, stored in *K*, was admitted to the quartz tube *Q* by the tap *N* at a pressure controlled by the capillary *L* and the temperature of a bath surrounding *K*, and measured with the butyl phthalate manometers *O* and *S*. The keten was dissociated either thermally or photochemically in the quartz tube, passed over metallic mirrors formed from the metal contained in the reservoir *Z*, and the unchanged keten and reaction products condensed out in *T*, which was immersed in liquid air. Pure hydrogen, to assist in the fashioning of the metal mirrors, was available through *M*.

FIG. 1.




*Production and Identification of Methylene.*—The experimental procedure was essentially the same as that described in previous communications from this laboratory (J., 1934, 1718; 1935, 1151; 1936, 253, 1777; 1937, 567). It was soon found that the products from keten would not remove cold tellurium mirrors, owing no doubt to the deposition of a thin deposit of polymer on the surface of the metal, an effect previously observed (Pearson and Purcell, J., 1935, 1151) in connection with the photo-dissociation of acetaldehyde. We therefore wound a few turns of No. 36 nichrome wire (2 mm. between the threads) round the tubes, and by means of a rheostat kept the temperature at 70—80°. The mirrors were then rapidly attacked by keten irradiated with the light from a cold or a hot mercury arc. To prove that the attack was due solely to the decomposition product, the following tests were made: (I) the mirror was heated in a vacuum for 30 mins., but no thinning was noticeable; (ii) keten was then passed over the heated mirror for long periods, but no removal resulted. That heating was essential was shown by passing keten for 5 secs. over a fresh, cold mirror, which was then heated, and the keten irradiated, but the mirror remained quite unaffected. All these experiments were repeated several times with fresh mirrors.

The identification of the radical proved as troublesome as usual, and experimental difficulties were aggravated by the conflicting opinions concerning methylene telluride (telluroformaldehyde). The red modification could not be produced in the ready manner described by Rice and Glasebrook (*loc. cit.*). Keten was distilled back and forth many times, and although large mirrors were being constantly removed, no trace of red solid was deposited anywhere in the quartz tube. A little trough was therefore built round the tube just behind the mirror and filled with solid carbon dioxide. After eight runs of keten, equivalent to 3 hours' irradiation, the bath was removed. The interior of the quartz tube was coated with a layer of deep orange, fluorescent solid, which was evidently Rice's red modification: it could be distilled in a high vacuum at 100° with slight decomposition, was insoluble in water, alcohol, and ether, and had the unpleasant odour subsequently found to be associated with all modifications of telluroformaldehyde. The layer of telluroformaldehyde could be formed anywhere in the quartz tube by cooling with carbon dioxide snow. On cooling the tube for only 15 mins., no solid could be observed, but as the photodissociation was continued, it gradually accumulated at the place where the bath had been. Thus it seems that the formation of the polymer required "seeding."

In addition to the red compound, a solid had formed in the liquid-air trap, colourless at −70°, and turning pale grey-green at room temperature. It had the penetrating organo-

metallic odour typical of telluroformaldehyde, quite distinct from dimethyl telluride and hydrogen telluride; it was readily soluble in acetone, chloroform, and ether, and darkened on exposure to air. The acetone or chloroform solutions rapidly decolourised iodine solutions, with the formation of methylene iodide. Attempts were first made to identify the methylene iodide in the manner used by Belchetz, *viz.*, by the addition of mercury. Belchetz claimed to have obtained the compound $CH_2I_2Hg$, m. p. 230°. Our repeated efforts failed to isolate it. We tried in vain to synthesise it from authentic methylene iodide, but obtained substances with various m. p.'s, all well below 230°. Finally, Sakurai's paper was consulted, and it was found that, in agreement with our observations, the reaction takes days for completion, yields two compounds, $CH_2I_2Hg$ and $CH_2I_2Hg_2$, which are insoluble in all the usual solvents, and can only be separated in methylene iodide.

We therefore identified the methylene iodide by converting it into formaldehyde, and tested for the latter by means of the Schryver–Rimini reaction. The necessary runs were made, and in the absence of air, iodine and chloroform were introduced by distillation. The trap was removed, the products allowed to react, and the excess of iodine removed by shaking with pure mercury. The yellow mercurous iodide and excess of mercury were filtered off, the clear solution evaporated on the water-bath, the residue moistened with chloroform, poured into a micro-Carius tube, and the chloroform again removed by evaporation. A little lead oxide and 0·5 c.c. of water were added, the tube was sealed, and heated in the furnace to 180° for about an hour. After cooling, the contents were filtered into a test-tube containing 2 c.c. of 1% aqueous phenylhydrazine hydrochloride and 1 c.c. of 5% potassium ferricyanide. On addition of 5 c.c. of concentrated hydrochloric acid an intense violet colour at once appeared, showing the presence of formaldehyde. The extreme sensitivity of this reaction led us to make two careful blank experiments. (i) In the first, chloroform and iodine were frozen in the trap *T* together with a little keten, the mixture warmed to room temperature, and an excess of iodine added, followed, in due course, by a drop of mercury; after shaking to remove the iodine, the filtered solution was evaporated to a small bulk in the water-bath, transferred to a micro-Carius tube, evaporated to dryness, treated with lead oxide and water, and heated. (ii) A second Carius tube was prepared in the same way, the keten being omitted. In neither experiment was a coloration obtained even after several hours' standing.

One further observation must be mentioned: the amounts of red and grey telluroformaldehyde taken together were obviously insufficient to account for the whole of the tellurium removed by the radicals, and it was found that on preserving the residual keten for a few days in liquid air, it left a substantial white deposit on evaporation, which did not redissolve readily in keten. It was similar in appearance, odour, and solubility to the white modification already described, but was contaminated with a considerable amount of polymerised keten, as indicated by a micro-carbon and -hydrogen analysis which gave values agreeing with the formula $TeCH_2,12\frac{1}{2}CH_2{:}CO$.

It is evident, therefore, that telluroformaldehyde is first generated as a gas, which undergoes the familiar aldehydic condensations to a white form and a red form, the latter, in view of its solubility, being the higher polymer. We were unable to detect methyl radicals in any of these experiments.

Inability to synthesise an authentic specimen of telluroformaldehyde led us to examine the selenium analogue, a polymeric form of which had been described by Vanino and Schinner (*J. pr. Chem.*, 1915, **91**, 116) as white columnar crystals, m. p. 215°, turning light green on exposure to sunlight (see also Brandt and Valkenburgh, *Proc. Indiana Acad. Sci.*, 1929, **39**, 165). We prepared it in good yield by passing hydrogen selenide at the rate of 2 bubbles per second for 1½ hours into a mixture of 40% formaldehyde (10 c.c.) and concentrated hydrochloric acid (30 c.c.). The white precipitate of selenoformaldehyde was filtered off, washed with much water, and recrystallised from a large volume of alcohol. It was deposited in very pale yellow needles, which became pale green on exposure to light. It had a garlic odour similar to that of telluroformaldehyde but somewhat less repulsive, and dissolved, on prolonged boiling in ether, acetone, and chloroform. Under the microscope, long polarising needles and clusters of small opaque granules were observed. The clusters melted at 66°, and began to distil away at 140°, whereas isolated needles melted between 200° and 220°. A crystallised sample one week old still showed the two modifications. After 3 weeks, however, there was no sign of melting at 66°, and complete melting at 206°. Selenoformaldehyde, therefore, separates in a metastable form, m. p. 66°, which slowly reverts to the stable modification, m. p. 205—215°.

Solutions of selenoformaldehyde in acetone react to give insoluble compounds with solutions of certain salts: mercuric chloride gives a pale yellow precipitate, which begins to char at 190°,

and is completely black by 230°. Mercuric bromide and iodide respectively give yellow and bright yellow precipitates which behave in a similar fashion. These compounds are more insoluble than the corresponding dimethyltelluride mercuric iodides, and on slow crystallisation form clusters of needles similar to the lactosazones. Silver nitrate gives a yellowish-brown, and palladous chloride a greenish-brown precipitate, but lead nitrate, 2 : 4-dinitrophenylhydrazine, semicarbazide, and picric acid are without action.

Since keten was to be present in our actual experiments, we used it as a solvent for some synthetic crystalline selenoformaldehyde which consisted almost wholly of the columnar crystals having the higher m. p. To allow time for any polymerisation processes, the solution was kept at −70° for some hours. The keten was removed by distillation, and a sample of the residue examined on the heating block under the microscope. The selenoformaldehyde now consisted of a mixture of polarising columnar crystals and opaque granular clusters. The granules began to melt at 60°, and finished melting at 68°, whilst the polarising needles melted at about 190°. Evidently, keten assists the formation of the lower-melting modification.

Selenium mirrors, even cold ones, were readily removed by the radicals from photolysed keten, but were not attacked by keten in the absence of light. The products of reaction collected only in the liquid-air trap, and could not be subsequently removed by distillation, so polymerisation was rapid and complete. After removal of the keten by distillation, the trap contained a pale greenish-yellow viscid solid, identical in odour with selenoformaldehyde. It was sparingly soluble in boiling alcohol, and from the solution, granular crystals were obtained by cooling. On heating, the edges of most of the crystals began to soften at 62°. At 66° these were completely melted. A residue of tiny polarising crystals remained which began to melt at 202° and were completely molten at 210°. This behaviour, identical with that of synthetic selenoformaldehyde which had been recrystallised from keten, was verified in a mixed m. p. determination.

From these observations it is clear that selenoformaldehyde, like telluroformaldehyde, exists first as a gas and polymerises to the two solid forms, m. p.'s 62—68° and 205—215°. The keten does not appear to act entirely as a solvent, for selenoformaldehyde crystallised from it no longer yields a precipitate with mercuric iodide.

The rate of decay of methylene was measured by observing the times of removal of warm standard tellurium mirrors situated at various distances from the irradiated zone in the quartz tube. Our first measurements served to show that we were dealing with a fragment of exceptionally long life. The quartz tube was 35 cm. long, and in this the time of removal of the mirrors was independent of their position in the tube. A fresh quartz tube 1 m. long was therefore built into the system, and despite the increased length, we could observe no decay. The results are recorded below :

| | | | | |
|---|---|---|---|---|
| Distance of mirror from lamp, cm. .............. | 5·0 | 30·7 | 53·5 | 81·5 |
| Time of removal of mirror, secs. ..................... | 133 | 132 | 143 | 128 |

The streaming velocity, 811 cm./sec., was determined by weighing in potassium hydroxide solution the amount of keten which passed through the tube in a measured time.

Average diameter of quartz tube = 1·1 cm. Pressure in first manometer = 0·153 cm. Hg. Average pressure gradient = 0·000912 cm. Hg. Therefore, time taken to traverse 81 cm., calculated from Herzfeld's equation (Paneth and Lautsch, *Ber.*, 1931, **64**, 2702), is 0·05 sec.

Thus, in 0·05 sec. the concentration of methylene had not perceptibly diminished.

For the purposes of discussion (see below), it is desirable to estimate the amount of keten dissociated. This may be obtained from the data recorded for diazomethane, which was found to be 59% dissociated when it took 45 secs. to remove a standard mirror at the furnace mouth.

Velocity of stream of diazomethane = 0·00722 g./min.

$$\therefore \text{ Yield of } CH_2 \text{ radicals in 45 secs.} = 0{\cdot}00722 \times \frac{45}{60} \times \frac{59}{100} \times \frac{14}{42} = 0{\cdot}00106 \text{ g.}$$

Now, the average time of removal of the standard mirrors with keten = 134 secs.

∴ Yield of $CH_2$ in 134 secs. = 0·00106 g. = 0·000076 g.-mol. Total amount of keten passing in 134 secs. = 3·020 × 134/1095 = 0·370 g. = 0·0088 g.-mol.

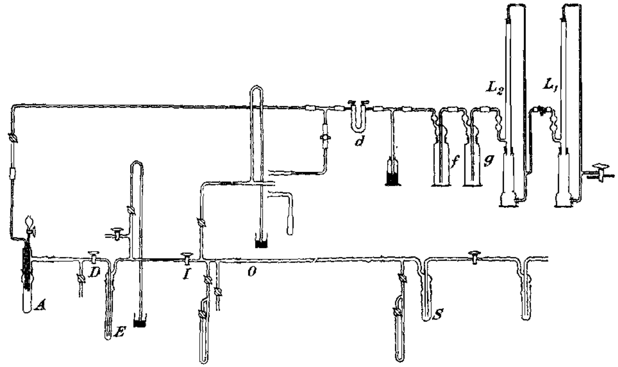
∴ Degree of dissociation = (0·000076 ÷ 0·0088) × 100 = 0·86%.

This estimate is almost certainly too high, for it assumes that all the diazomethane dissociated into free radicals; nevertheless, it is a safe value on which to base the later discussion.

The possibility arose that the long life of the molecule was due to the formation of a loose compound easily dissociated in contact with metallic mirrors, *e.g.*, $CH_2 + CH_2{:}CO \longrightarrow$ $\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix}\!\!>\!CO$. This compound exists only in solution, and any attempt to remove it results in a viscous polymer (Lipp, Buchkremer, and Seeles, *Annalen*, 1932, **499**, 1). It does, however, form a crystalline semicarbazone. Repeated attempts to prepare such a derivative from the fractionated products of the photolysis of keten were unsuccessful.

We were thus faced with the anomaly of a methylene radical short-lived in methane and diazomethane, and completely stable in keten. We therefore decided to investigate the radical obtained from diazomethane. The diazomethane was prepared by gradually adding nitrosomethylurethane (1 vol.) to a cold 6% solution of sodium in ethylene glycol (2 vols.) (Meerwein and Burneleit, *Ber.*, 1928, **61**, 1840), and since it had to be handled in the complete absence of air, the apparatus used in Fig. 2 was constructed. The preparation was effected in the vessel $A$, provided with a tap-funnel and delivery tube for admitting pure dry nitrogen, in which the

FIG. 2.




diazomethane was carried forward to the vessel $E$, containing purified, dry butyl phthalate or ether, cooled until viscous in a bath of carbon dioxide snow. After all the diazomethane had collected in $E$, the nitrogen was removed by closing $D$ and evacuating through $I$, the last traces being eliminated together with any volatile impurities by successively warming, cooling, and evacuating the vessel.

The nitrogen, since it was also to be used as a transport gas for free radicals, was carefully freed from oxygen in the towers $L_1$ and $L_2$ containing concentrated aqueous ammonia and spirals of copper gauze, and was washed with dilute sulphuric acid in $g$, syrupy phosphoric acid in $f$, and dried over phosphoric oxide in $d$.

The thermal decomposition of diazomethane was first investigated. Decomposition was effected by an electric furnace, 15 cm. long, surrounding the quartz tube close to $O$. The temperatures were read on a millivoltmeter connected with a platinum–platinum-iridium thermocouple calibrated against a platinum-resistance thermometer. Plentiful yields of active fragments were obtained from a stream of diazomethane vapour at 2 mm. pressure with or without ether as a carrier gas, but above 400°, decomposition was accompanied by the deposition of carbon within the heated zone, and with rising temperature, the yield of radicals began to diminish. This deposition of carbon was not recorded by Rice and Glasebrook (*loc. cit.*), but it accords with their observation that at higher temperatures methylene gives place to methyl; and accounts for the deposition of carbon in Williamson's experiments (*loc. cit.*).

The fragments, in the absence of a carrier gas, were identified by their reaction with elementary tellurium. A little red telluroformaldehyde was deposited behind the tellurium where

Rice and Glasebrook had obtained a plentiful yield, but as with the seleno- and the telluroformaldehyde from keten, polymerisation could be accelerated by surrounding the tube beyond the mirror with a bath of solid carbon dioxide. On removing the bath, we observed (*a*) an orange-yellow liquid which partly distilled, leaving a residue of orange-red solid, (*b*) a white deposit which, as the tube gradually reached the room temperature, partly melted to a colourless liquid, and ultimately volatilised. The behaviour was strikingly similar to that observed during the formation of polymers from ordinary aldehydes.

The diazomethane was then carefully distilled from the other products which had collected in the trap *S*, and the residue was preserved overnight in a bath of solid carbon dioxide. A few tiny droplets, some orange-coloured, some colourless, remained in the trap. They had a strong odour of telluroformaldehyde with a background of nitrogenous bases, but no methyl or hydrogen telluride was perceptible. With a solution of mercuric iodide in acetone, canary-yellow granules were immediately deposited. On heating, they turned red, and then decomposed leaving only a black residue at 300°, a behaviour so closely similar to that of selenoformaldehyde mercuric iodide that we felt confident in assuming that we were dealing with the tellurium analogue.

It is clear, therefore, that telluroformaldehyde, whether prepared in keten or diazomethane, is first formed as a gas and has at least two other polymers. In our experiments, the red one, deposited just behind the mirror, accounted for only a small part of the total yield, and in an endeavour to confirm Rice and Glasebrook's findings that it is the sole product, their experimental conditions were followed as closely as possible by using ether as a carrier gas, and adjusting the furnace temperature to 450°. Although large tellurium mirrors were rapidly consumed, we again obtained only a fraction of the telluroformaldehyde as the red polymer.

The products from the photodecomposition were next investigated. In accordance with the arguments of Norrish and Kirkbride (J., 1933, 119), we found that the hot mercury arc, rich in radiations about 3130 A., yielded scarcely any radicals, whilst a cold arc with its maximum intensity at 2580 A. gave plentiful yields comparable with those obtained by using the furnace. The products of the reaction with tellurium were as numerous; but a greatly improved yield of the fluorescent orange-red solid was deposited behind the mirror; again, however, it was not the sole product. Methyl radicals were not detected in either the photo- or the thermo-chemical decompositions of diazomethane at lower temperatures.

The life period of the radicals was measured in the usual way by using tellurium mirrors. The radicals were prepared thermally from a sample of diazomethane kept in butyl phthalate, *i.e.*, in the absence of a carrier gas. In view of the experimental difficulties, we could not obtain a direct estimate of the streaming velocity, and assumed that it was the same as that of pure ether, which we could measure. The following data were obtained:

| | |
|---|---|
| Temp. of furnace | 400° |
| Initial pressure | 0·8 cm. of butyl phthalate. |
| Final pressure | 0·4 cm. ,, ,, |
| Distance of furnace from end of tube | 72 cm. |
| Distance between manometers | 164·5 cm. |
| Diameter of tube | 1·1 cm. |
| Weight of ether passing through tube per min. | 0·161, 0·156, 0·163, mean 0·160 g. |
| ∴ Streaming velocity | 1180 cm./sec. |

The values for the times of removal of the mirrors are recorded in Table I, and prove that the radicals react according to a sensibly unimolecular law, and have a half-value period of $5·0 \times 10^{-3}$ sec.

TABLE I.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Distance from furnace mouth, *d* cm. | 14·3 | 6·2 | 27·3 | 21·6 | 18·4 | 25·4 | 10·6 |
| Time of removal, *t* secs.* | 40 | 21 | 127 | 75 | 65 | 92 | 29 |
| Time, $\tau$ sec., taken to traverse *d* cm.* | 0·0093 | 0·0041 | 0·0172 | 0·0136 | 0·0119 | 0·0161 | 0·0068 |

* The symbols *d*, *t*, and $\tau$ in subsequent tables have the same significance as in this table.

The experiments were repeated with the cold mercury arc in place of the furnace. The following two values sufficed to show the similar behaviour of the radicals, which have the half-value period $6·4 \times 10^{-3}$ sec.

| | | |
|---|---|---|
| *d*, cm. | 11·5 | 39·5 |
| *t*, secs. | 32 | 194 |
| $\tau$, sec. | 0·0073 | 0·0241 |

These data establish beyond doubt a profound difference in the behaviour of methylene prepared from and in the presence of keten and diazomethane severally. The unlikely suggestion that methylene may exist in two forms was discounted on two grounds: the half-value periods of the radical produced thermally and photochemically were identical, and the conversion from the $^3S$ into the $^3P$ state or *vice versa* should occur, as in the case of carbon monoxide, instantaneously, so that only one form, the more stable, would ever be detected in ordinary chemical manipulations. The different half-value periods must therefore be attributed to the presence of keten in the one case and diazomethane in the other. If methylene is intrinsically as reactive as methyl, then the apparent stability in keten is to be ascribed either (*a*) to the formation of an addition compound, which has already been disposed of as unlikely (see below), or (*b*) to the poisoning of the walls of the quartz tube by keten, so that the surface no longer functions as a catalyst for the formation of ethylene ($2CH_2 \longrightarrow C_2H_4$). We disposed of this possibility by passing keten through the tube prior to each of a series of measurements of a half value period in diazomethane. The half value was not perceptibly altered. As an additional confirmation, and to establish if possible our contention that the stabilisation in keten was not due to the formation of an addition compound, we examined the effect of passing keten and diazomethane simultaneously through the furnace heated to such a temperature that only the latter was dissociated.

The keten container was immersed in a bath of solid carbon dioxide and ether so that a constant vapour pressure could be maintained. After the formation of the standard mirror, the keten stop-cock was opened slowly until the desired pressure was attained (we had previously ascertained the inactivity of the keten at the temperature of the furnace). When conditions became stable, the diazomethane stop-cock was opened until a second rise of 2 mm. was registered in the manometer limbs. Times of disappearance of mirrors were obtained for partial pressures of 2 mm. and 10 mm. of keten, the value for diazomethane being kept at 2 mm. No direct measurements were obtained for the streaming velocities at these pressures. The figures given below were extrapolated from values observed for pure ether.

| | | |
|---|---|---|
| Total pressure, mm. of butyl phthalate ............ | 4 | 10 |
| Streaming velocity, cm./sec. ............................ | 730 | 2000 |
| Pressure gradient, mm. of butyl phthalate ......... | 0·00122 | 0·00304 |

TABLE II.

*Partial pressure of keten, 2 mm.*

| | | | | |
|---|---|---|---|---|
| *d*, cm. .................................... | 11·8 | 13·0 | 40·7 | 41·3 |
| *t*, secs. .................................... | 80 | 95 | 384 | 346 |
| $\tau$, sec. .................................... | 0·0123 | 0·0135 | 0·0399 | 0·0407 |

Half-value period = $13·4 \times 10^{-3}$ sec.

*Partial pressure of keten, 10 mm.*

| | | | |
|---|---|---|---|
| *d*, cm. .................................... | 11·8 | 40·5 | 41·5 |
| *t*, secs. .................................... | 94 | 106 | 112 |
| $\tau$, sec. .................................... | 0·0045 | 0·0145 | 0·0149 |

Half-value period = $50 \times 10^{-3}$ sec.

The results show that the half-value period was considerably extended by the addition of keten, and it now remained to be discovered whether this effect was due to dilution, and could be just as well achieved by the use of inert substances such as ether and nitrogen.

The diazomethane was collected in ether which had been previously dried over sodium. After each series of measurements the concentration of diazomethane was decreased either by pumping out at $-80°$ or by diluting a portion of the solution with ether. The initial pressure was kept throughout at 8 mm. of butyl phthalate. The results are in Table III.

The half-value periods obtained from these results are, respectively, 9, 11, 17, and $30 \times 10^{-3}$ sec. There is a definite increase in the life period with increase in the ratio ether/diazomethane.

The passage of nitrogen through the apparatus was found to be slow, owing to the fact that the gas does not condense in the liquid-air trap. The difference in pressure between the two manometers was accordingly small, and cathetometers had to be used to observe the liquid levels. A graph was constructed from a number of readings so that the relation between the two pressures could be obtained. To obtain the rate of passage of the gas, nitrogen was stored in a Bunte gas burette, and the volumes passing over in given times at various initial pressures were measured. A graph was constructed showing the relation between pressure and c.c. at *N.T.P.*

TABLE III.

*Temperature of furnace,* 440°.

| | | | | |
|---|---|---|---|---|
| *d*, cm. | 6·3 | 6·5 | 38·3 | 39·7 |
| *t*, secs. | 17 | 18 | 72 | 89 |
| $\tau$, sec. | 0·0041 | 0·0043 | 0·0236 | 0·0243 |

*Temperature of furnace,* 430°.

(Relative concentration of $CH_2N_2$ had been reduced by pumping out at 1 cm. of butyl phthalate for 20 mins.).

| | | | |
|---|---|---|---|
| *d*, cm. | 12·2 | 37·4 | 38·3 |
| *t*, secs. | 23 | 56 | 66 |
| $\tau$, sec. | 0·0070 | 0·0231 | 0·0236 |

*Temperature of furnace,* 430°.

(Diazomethane concentration reduced by dilution with 1½ times the volume of ether present.)

| | | | | |
|---|---|---|---|---|
| *d*, cm. | 13·8 | 13·8 | 38·5 | 41·1 |
| *t*, secs. | 43 | 38 | 74 | 89 |
| $\tau$, sec. | 0·0089 | 0·0089 | 0·0234 | 0·0251 |

*Temperature of furnace,* 420°.

(Carried out after further dilution with 2 vols. of ether.)

| | | | | | |
|---|---|---|---|---|---|
| *d*, cm. | 12·5 | 13·3 | 41·5 | 41·9 | 40·8 |
| *t*, secs. | 139 | 168 | 210 | 220 | 249 |
| $\tau$, sec. | 0·0080 | 0·0087 | 0·0252 | 0·0255 | 0·0249 |

A mixture of nitrogen at 2 mm. of butyl phthalate and diazomethane at the same pressure was then passed through the furnace at 420°, and times of disappearance of tellurium mirrors observed. To calculate the streaming velocity, it was assumed that the conditions of flow were those in pure nitrogen.

Manometer readings: 4 mm. and 3·8 mm. of butyl phthalate. Volume of $N_2$ passing at 4 mm. = 0·35 c.c./min. Streaming velocity $= \frac{0\cdot35}{60} \times \frac{76}{0\cdot4} \times 13\cdot6 \times \frac{1}{3\cdot14(0\cdot55)^2} = 15\cdot8$ cm./sec. Pressure gradient = (0·4 − 0·38)/164·5 = 0·000122.

TABLE IV.

| | | | | |
|---|---|---|---|---|
| *d*, cm. | 6·3 | 7·5 * | 12·8 | 13·5 |
| *t*, secs. | 47 | 35 | 139 | 140 |
| $\tau$, sec. | 0·387 | 0·460 | 0·785 | 0·828 |

Half-value period = 230 × $10^{-3}$ sec.

I

D.

* Pressure of $CH_2N_2$ slightly over 2 mm.

Di..se results show that there is no reason to discriminate between the effect of ether, nitrogen,
Wei..n in prolonging the life of methylene. They function as pure diluents, which retard
∴ St ion of the molecules to the walls of the vessel, where they may also compete for the
The values dsorptive surface. The short life period in pure diazomethane must therefore be
radicals react reaction between methylene and diazomethane. This conclusion was tested by
$10^{-3}$ sec. ow the rate of disappearance of the radicals varied with the initial methylene

Distance from furnace ane was passed through the furnace at an initial pressure of 2 mm. of butyl
*d* cm. ................. eriod measurements were made for the series of temperatures listed below.
Time of removal, *t* secs. elocity of ether at 2 mm. was taken as equivalent to that of diazomethane.
Time, $\tau$ sec., taken to tras collected in the trap in 15 mins. Pressure gradient = 0·00122 cm. of
*d* cm.* ..................... he streaming velocity is, therefore, 375 cm./sec.

* The symbols *d*, *t*, an V are shown in Fig. 3, where the lowest straight line *A* represents the
ounced curves *B* and *C* those for 422° and 495°, and the flatter line *D*

The experiments were ° the initial concentration of radicals begins to diminish, and the values
following two values suffice e figure to avoid confusion, as they merely confirm the general trend
value period 6·4 × $10^{-4}$ sec nperatures to become linear.

e data, it was desirable to know how the quantity of diazomethane
*d*, cm. he temperature. A quantity of diazomethane at 2 mm. (butyl
*t*, secs.
$\tau$, sec. igh the furnace at various temperatures for a measured time. The

TABLE V.

*Furnace temperature, 392°.*

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| *d*, cm. ... | 3·2 | 7·7 | 11·5 | 14·7 | 14·8 | 24·9 | 27·2 | 36·7 | 39·0 | |
| *t*, secs. ... | 57 | 82 | 103 | 157 | 218 | 295 | 295 | 570 | 582 | |
| *τ*, sec. ... | 0·0049 | 0·0110 | 0·0162 | 0·0198 | 0·0201 | 0·0321 | 0·0354 | 0·0435 | 0·0461 | |

Half-value period = $12 \times 10^{-3}$ sec.

*Furnace temperature, 422°.*

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| *d*, cm. ... | 4·2 | 4·0 | 7·2 | 8·1 | 8·5 | 13·5 | 17·8 | 18·2 | 34·2 | 34·4 |
| *t*, secs. ... | 14 | 10 | 38 | 46 | 45 | 87 | 122 | 127 | 363 | 368 |
| *τ*, sec. ... | 0·0064 | 0·0059 | 0·0106 | 0·0117 | 0·0122 | 0·0187 | 0·0237 | 0·0248 | 0·0422 | 0·0427 |

*Furnace temperature, 495°.*

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *d*, cm. ... | 5·0 | 5·5 | 8·0 | 13·5 | 14·7 | 23·5 | 35·2 | 37·2 |
| *t*, secs. ... | 10 | 13 | 21 | 48 | 55 | 171 | 309 | 298 |
| *τ*, sec. ... | 0·0073 | 0·0080 | 0·0114 | 0·0187 | 0·0198 | 0·0307 | 0·0430 | 0·0449 |

*Furnace temperature, 525°.*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *d*, cm. ... | 4·7 | 5·5 | 7·7 | 9·2 | 19·0 | 19·6 | 36·5 |
| *t*, secs. ... | 8 | 6 | 15 | 16 | 90 | 69 | 352 |
| *τ*, sec. ... | 0·0065 | 0·0080 | 0·0110 | 0·0131 | 0·0251 | 0·0264 | 0·0439 |

*Furnace temperature, 595°.*

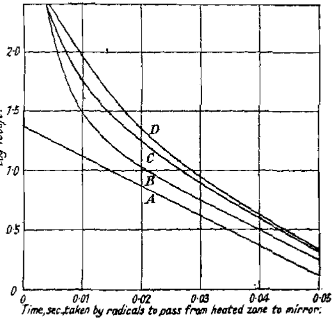
| | | | | | |
|---|---|---|---|---|---|
| *d*, cm. ... | 4·3 | 5·5 | 10·4 | 18·7 | 32·2 |
| *t*, secs. ... | 13 | 6 | 25 | 84 | 388 |
| *τ*, sec. ... | 0·0063 | 0·0080 | 0·0145 | 0·0247 | 0·0402 |

gas was collected in the trap into which had been frozen a small amount of ether. On being warmed slightly, the ether melted and dissolved the condensate. The trap was opened, and the contents quickly poured into a colorimeter. The intensity of the colour was compared with that of a solution of potassium chromate. By comparing the relative concentrations at various temperatures with that at room temperature, an estimate of the percentage decomposition was obtained:

| | |
|---|---|
| Decomposition at 400° .............. | 67% |
| ,, ,, 495° .............. | 77% |

Since the percentage decomposition is so high, appreciable quantities of nitrogen are formed, so it is necessary to introduce a correction for (*a*) the increased pressure and (*b*) the diminished streaming velocity. The furnace was brought to 495° until stable conditions of flow were obtained. The furnace was then suddenly cooled in a rapid air stream. The pressure decreased by 20%. This means that at room temperature we were running an excess of 20% of diazomethane. This correction brings the above values to 59 and 71% at 400° and 495° respectively. These values show that the 100-fold increase in methylene observed between 392° and 422° in Fig. 3 is not accompanied by a corresponding increase in the amount of diazomethane dissociated.

FIG. 3.




A *curve for* 392°; B *for* 422°; C *for* 495°; D *for* 525°.

The interpretation of the graphs in Fig. 3 can now be attempted. If the methylene disappears in a bimolecular reactions with diazomethane, these curves should be expressed by the general law

$$-dx/dt = K[a - (x_0 - x)] = K(B + x)$$

where $x$ = concentration of the methylene at time $t$, $x_0$ and $a$ are the initial concentrations of methylene and diazomethane respectively (*i.e.*, at $t = 0$), and $B = a - x_0$. Integrating between the limits $x_0$ and $x$, we have

$$[\log_e x(B + x_0)/x_0(B + x)]/B = Kt$$

When $a$ is large compared with $x_0$, this reduces to $(\log_e x/a)/a = K't$, and the values follow the unimolecular law, *i.e.*, the straight line $A$ at 392°. When $a$ is comparable with $x$, the plot of $\log_e x$ against $t$ must yield curves such as $B$ and $C$; and the flatter curve $D$ is due, once more, to the diminution in $x_0$. The conclusion must therefore be drawn that the decay of methylene is due to a reaction with diazomethane, which, from the experiments in the presence of diluent gases, probably occurs on the surface of the quartz tube.

There is no reason, therefore, to regard methylene as anything other than a reactive molecule. In particular it does not possess that property which discriminates a free radical from other molecules, *viz.*, that of combining readily with itself to yield a stable dimeric form. Thus, in our experiments with keten, each molecule suffered no less than $3 \times 10^3$ collisions with the wall of the tube and $4 \times 10^5$ collisions with other molecules in passing along the quartz tube without signs of reaction.

It was finally decided to measure the activation energy of the reaction responsible for production of free radicals from diazomethane by observing how the yield of radicals (at the furnace mouth) varied with the temperature. The experiments were made with ether as a carrier gas to avoid as far as possible differences in streaming rate due to the different proportions of nitrogen produced from diazomethane at different temperatures. The results are recorded in Table VI.

TABLE VI.

*Temperature*, 387° (660° K.).

| | | | |
|---|---|---|---|
| $d$, cm. | 13·7 | 14·4 | 37·9 |
| $t$, secs. | 130 | 140 | 256 |
| $\tau$, sec. | 0·0088 | 0·0094 | 0·0232 |

*Temperature*, 430° (703° K.).

| | | | | |
|---|---|---|---|---|
| $d$, cm. | 13·8 | 13·8 | 36·5 | 41·1 |
| $t$, secs. | 38 | 43 | 74 | 89 |
| $\tau$, sec. | 0·0089 | 0·0089 | 0·0234 | 0·0251 |

*Temperature*, 525° (798° K.).

| | | | | | | |
|---|---|---|---|---|---|---|
| $d$, cm. | 7·2 | 10·2 | 11·6 | 22·5 | 24·5 | 30·3 |
| $t$, secs. | 10 | 13 | 16 | 32 | 38 | 63 |
| $\tau$, sec. | 0·0047 | 0·0066 | 0·0074 | 0·0142 | 0·0154 | 0·0190 |
| $d$, cm. | 32·5 | 35·0 | 38·6 | 43·0 | 43·5 | 44·0 |
| $t$, secs. | 80 | 81 | 81 | 97 | 110 | 113 |
| $\tau$, sec. | 0·0200 | 0·0217 | 0·0235 | 0·0261 | 0·0263 | 0·0267 |

The extrapolated values of log $1000/t$ at the mouth of the furnace (distance 8·0 cm.) are recorded below, and give as the apparent activation energy, determined graphically, 22 kg.-cals.

| | | | |
|---|---|---|---|
| Temp., K. | 660° | 703° | 798° |
| log $1000/t$ | 1·05 | 1·57 | 2·20 |

An interesting feature of these experiments is that a unimolecular law is followed by the radicals in the experiments at the higher temperatures. If the conclusions previously discussed, concerning the mode of disappearance, are correct, the unimolecular decomposition would only occur if the quantity of diazomethane decomposed in these experiments were small. It was found that even at 430° only 9% of the diazomethane had been dissociated. It thus appears that the ether prevents the propagation of some chain process responsible for the large dissociation (*ca.* 60%) in the pure gas.

## SUMMARY AND CONCLUSIONS.

Methylene has been prepared by the thermal dissociation of diazomethane, and by the photodissociation of diazomethane and keten, and has been detected by its reactions with tellurium and selenium, whereby telluro- and seleno-formaldehydes are formed. They are first produced as vapours, which subsequently polymerise to give in each case at least two solids. Tellurium gives the characteristic orange-red form previously described by Rice; and a greyish-white form which has some resemblance to that claimed by Belchetz, but subsequently regarded as a mixture of hydrogen telluride and tellurium. We cannot agree with Rice that the sole reaction product of methylene and tellurium consists of the red

telluroformaldehyde, and his criticism of Belchetz's work on this ground, and in the belief that telluroformaldehyde could not have passed from the mirror to the liquid-air trap, can no longer be upheld.

It has been found that, whereas methylene has a half-value period of $5 \times 10^{-3}$ sec. in the presence of diazomethane (Table I), there is no measurable decay in the presence of keten even in $50 \times 10^{-3}$ sec. The half-value period in diazomethane can be extended by dilution with keten (Table II), an effect which is due neither to the poisoning of the walls of the tube by the keten, with the consequent suppression of the association process $2CH_2 \longrightarrow C_2H_4$, nor to the formation of a loose complex of methylene and keten, but to an ordinary dilution effect which can be equally well realised with ether (Table III) or nitrogen (Table IV). In the presence of the latter, the half-value period has been increased to $230 \times 10^{-3}$ sec., and this has been ascribed to the suppression of a wall reaction, which suppression may be very efficient in a tube under conditions of stream-line flow.

The short life period in diazomethane is due to a bimolecular reaction between diazomethane and methylene, revealed in a study of the kinetics of the decay of methylene in various initial concentrations of diazomethane either alone (Table V), or diluted with ether (Tables III and VI).

These results give a good reason for the difference in quantum yields obtained for keten (Ross and Kistiakowsky) and diazomethane (Norrish and Kirkbride). We have shown that reactions between methylene and keten must be very slow, so that the methylene first formed is probably removed by association. In our opinion this view accords better with Ross and Kistiakowsky's interpretation than with that of Norrish and Kirkbride because (*a*) each methylene survived $4 \times 10^5$ collisions with keten in our quartz tube, and (*b*) we do not think that the quantum yields observed by Ross and Kistiakowsky, which have a mean value of 1·08, can be safely assumed to exceed unity in view of the errors inherent in such measurements. In the case of diazomethane, the reaction with methylene is so rapid that the quantum yield must be 2 even in the absence of secondary reactions. That such secondary reactions are probable may be seen from the influence of ether in inhibiting reaction chains in the furnace, so that a quantum yield of 4—5 is not surprising, and confirms the findings of Kirkbride and Norrish.

The controversy between Belchetz and Rideal, on the one hand, and Rice and his colleagues on the other, appears to have been provoked by a misapprehension which the present experiments dispel. Although there is no reason to suspect a rapid reaction between methylene and methane at room temperature, for Kassel suggests an energy increment of 44 kg.-cals. for the reaction, and we find no reaction between methylene and ether, yet above 800°, as in the furnace used by Rice or with the activated methane molecules doubtless present in Belchetz's gases as they left the filament, a reaction must be possible, and would account for the inability of Rice *et al.* to detect methylenes at all, and of Belchetz to obtain them when his detector mirrors were situated at distances greater than the mean free path from the heated filament. The preparation of methylene from diazomethane below 400° is not surprising. Above 500° it would be, but for the occurrence of the chain reaction in the furnace which more than compensates for the tendency of the radicals to dissociate and to interact with other species until the temperature exceeds 600°, when only methyls are detectable (Rice and Glasebrook, *loc. cit.*).

The possibility that methylene is a primary product of the dissociation of methane, in agreement with the postulates and experiments of Nef, Bone and Coward, and Kassel, is thus once more open, and if this present justification of Belchetz and Rideal's work be valid, the occurrence of methylene must be held to be at least more likely than that of methyl.

The failure of Paneth and Lautsch (*loc. cit.*) to detect methylene in the thermal or electrical dissociation of diazomethane, and possibly in the reaction between methylene chloride and sodium vapour, must be ascribed to their choice of carbon and benzoic acid as detectors, for there is nothing to lead us to suspect that a rapid reaction should occur between either of them and methylene.

The whole of our experimental results accord with the view (see p. 413) that in methylene the carbon is essentially bivalent; the molecule has none of those properties which one

would naturally associate with the highly unsaturated, and therefore reactive, species $>CH_2$.

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## 83. *Some Symmetrical Acylarylureas.*

By EDWARD N. ABRAHART.

The preparation of *s*-benzoyl- and *s*-*p*-nitrobenzoyl-arylureas by general methods proceeds normally; on the other hand, that of *s*-3-hydroxy-2-naphthoylarylureas is complicated by side reactions in both of the methods employed. 3-Hydroxy-2-naphthoyl chloride readily condenses with itself to give a resinous product of depside properties and hence poor yields are obtained by the direct acylation of arylureas. The condensation of *3-hydroxy-2-naphthoylurea* with aniline under certain conditions leads to ring-closure in the 2 : 3 position with the formation of a diketo-oxazine. Normal condensation occurs with an excess of aniline and a shorter period of heating.

THE benzoyl and 3-hydroxy-2-naphthoyl derivatives of certain monoarylureas have been prepared by two general methods, *viz.*, by the interaction of the acyl chloride and an arylurea (cf. Walther and St. Włodkowski, *J. pr. Chem.*, 1899, **59**, 273 *et seq.*) and by the condensation of a monoacylurea with an arylamine at 160—170° (Palit, *J. Indian Chem. Soc.*, 1934, 479).

The *s*-*p*-nitrobenzoyl derivatives of phenyl-*o*-tolyl- and -*p*-tolyl-ureas have been obtained by acylation in pyridine at 100°, but all attempts to prepare the corresponding 3-hydroxy-2-naphthoyl compounds by similar means failed owing to the auto-condensation of the whole of the hydroxy-acid chloride, with the loss of hydrogen chloride. The decomposition product, a yellow amorphous powder containing no chlorine, was insoluble in cold alkali solution, hydrolysed by boiling to 3-hydroxy-2-naphthoic acid, and gave the anilide when boiled with aniline. In these and other properties the product closely resembles that obtained by the prolonged heating of 2-acetoxy-3-naphthoic acid (Meister Lucius and Bruning, *Chem. Zentr.*, 1916, II, 1094) (cf. "disalicylides" and other products obtained by heating *o*-acetoxybenzoic acid under reduced pressure; Anschütz, *Ber.*, 1919, **52**, 1883). Decomposition, giving a similar product, occurs when the acid chloride is heated at or above its melting point.

In its properties and modes of formation this product appears to be a depside or mixture of depsides, produced by the interaction of the OH and COCl groups of at least two molecules of the chloride (cf. di- and poly-salicylide from salicylic acid and phosphoryl chloride in pyridine; Einhorn and Mettler, *Ber.*, 1902, **35**, 3646; Anschütz, *ibid.*, p. 3506).

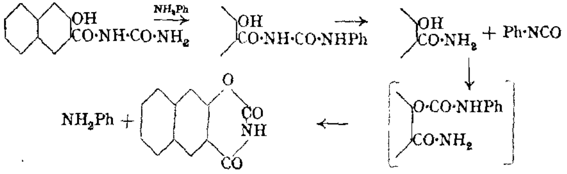
*s*-3-Hydroxy-2-naphthoylarylureas have, however, been prepared by heating the acid chloride and arylureas in dry benzene under reflux conditions. Approximately 60% of the acid chloride undergoes auto-condensation.

The observation of Kuhn (*Ber.*, 1884, **17**, 2881) that acylarylureas decompose at high temperatures (200°) into an amide and an *iso*cyanate has been verified by heating benzoyl- and *p*-nitrobenzoyl-arylureas with aniline at 200°, benzamide, or its derivative, and a diarylurea being formed :

$$R\cdot CO\cdot NH\cdot CO\cdot NHR' \longrightarrow R\cdot CO\cdot NH_2 + R'\cdot NCO;\ R'\cdot NCO + NH_2Ph \longrightarrow R'\cdot NH\cdot CO\cdot NHPh$$

a mechanism which is assumed by Palit (*loc. cit.*) in explaining the products obtained by the prolonged heating of acetylurea and aniline. When 3-hydroxy-2-naphthoylurea and aniline were heated together in equimolecular quantities for 3 hours at 170—180°, ammonia was evolved and 2 : 4-diketo-3 : 4-dihydro-ββ-1 : 3-naphthoxazine (Fries, *Ber.*, 1925, **58**, 2845) was obtained. Einhorn and Schmidlin (*Ber.*, 1902, **35**, 3653) obtained the corres-

ponding benzene derivative by the action of phenyl *iso*cyanate on salicylamide, and it seems likely that the naphthalene analogue is produced by the following mechanism:




When heated for a short time with an excess of aniline, 3-hydroxy-2-naphthoylurea afforded *s-3-hydroxy-2-naphthoylphenylurea* in good yield.

## Experimental.

*s-Benzoyl-o-tolylurea.*—Benzoylurea (2 g.; 1 mol.) and *o*-toluidine (1·3 g.; 1 mol.) were heated together at 170—175° during 2 hours; the evolution of ammonia then ceased. The brown solid was freed from unchanged base by steam-distillation, and the hot aqueous solution rapidly filtered; the cooled filtrate deposited benzoylurea. The undissolved *s*-benzoyl-*o*-tolylurea crystallised from glacial acetic acid in colourless needles (1·9 g.), m. p. 211° (Walther and St. Wlodkowski, *loc. cit.*, give m. p. 210°; Gattermann and Cantzler, *Ber.*, 1892, **25**, 1089, m. p. 210°).

*s*-Benzoylphenylurea was obtained, when aniline was used, in 65% yield, m. p. 205°; Palit (*loc. cit.*) gives m. p. 204—205, and 51% yield. When heated with aniline at 220°, it gave benzamide and *s*-diphenylurea, m. p. and mixed m. p. 235°. When benzoylurea and ethylaniline were heated together in molecular quantities at 170—175°, no ammonia was evolved and the reactants were recovered unchanged.

*s-Benzoyl-o-chlorophenylurea*, fine colourless needles, m. p. 212°, from acetone (yield, 50%) (Found: N, 10·1. $C_{14}H_{11}O_2N_2Cl$ requires N, 10·2%), and *s*-benzoyl-*p*-chlorophenylurea, colourless needles, m. p. 232°, from glacial acetic acid (yield, 62%) (Stieglitz and Earle, *J. Amer. Chem. Soc.*, 1908, **30**, 416, give m. p. 235—237°), were obtained similarly.

*s-p-Nitrobenzoylphenylurea.*—(a) *p*-Nitrobenzoylurea (Jacobs and Heidelberger, *J. Amer. Chem. Soc.*, 1917, **39**, 1436) (2 g.; 1 mol.) was heated with aniline (1 g.; 1 mol.) at 165° during 2½ hours. The brown solid was subjected to steam-distillation, and the residue, which contained unchanged *p*-nitrobenzoylurea, was crystallised several times from glacial acetic acid; the pale yellow plates, m. p. 232°, obtained were identical with those described below. At 180°, the products were *p*-nitrobenzamide (yellow needles from water, m. p. 198°) and *s*-diphenylurea (needles from acetone, m. p. and mixed m. p. 235°).

(b) *p*-Nitrobenzoyl chloride (3 g.) was gradually added to a cold solution of phenylurea (2·2 g.) in pyridine (10 c.c.). The bulky precipitate dissolved completely on heating and after 1 hour the clear red solution was cooled, water added, and the colourless precipitate washed with cold acetone. The *product* crystallised from glacial acetic acid in pale yellow plates, m. p. 232°, undepressed by the specimen described above (Found: C, 59·5; H, 4·0. $C_{14}H_{11}O_4N_3$ requires C, 59·0; H, 3·9%). When heated with aniline at 200°, it gave *p*-nitrobenzamide and *s*-diphenylurea.

*s-p-Nitrobenzoyl-o-tolylurea.*—(a) *p*-Nitrobenzoylurea (2·0 g.) and *o*-toluidine (1·1 g.) were heated together at 160—165° during 3 hours. The *product* was isolated as before and obtained in fine fibrous needles (1·4 g.), m. p. 219°, from glacial acetic acid (Found: C, 60·7; H, 4·3. $C_{15}H_{13}O_4N_3$ requires C, 60·2; H, 4·35%).

(b) *p*-Nitrobenzoyl chloride (1·75 g.) and *o*-tolylurea (1·5 g.) were heated together in pyridine (10 c.c.) at 100° during 1 hour. The product crystallised from glacial acetic acid in pale yellow, fibrous needles, m. p. 219°, and in admixture with the previous preparation 218—219°.

*s-p-Nitrobenzoyl-p-tolylurea.*—(a) *p*-Nitrobenzoylurea (2 g.) and *p*-toluidine (1·1 g.) were heated together at 165° during 3 hours; the *product* crystallised from glacial acetic acid in yellow plates (1·6 g.), m. p. 244° (Found: C, 60·7; H, 4·3%).

(b) *p*-Nitrobenzoyl chloride (1·75 g.), *p*-tolylurea (1·5 g.), and pyridine (10 c.c.) were heated

at 100° during 1 hour. The product crystallised from glacial acetic acid in yellow plates, m. p. 245°, and in admixture with the previous preparation had m. p. 244°.

s-*3-Hydroxy-2-naphthoylphenylurea.*—A solution of 3-hydroxy-2-naphthoyl chloride (6·3 g.; 1 mol.), m. p. 94·5° (prepared by the method of Meyer, *Monatsh.*, 1901, 22, 791, who gives m. p. 191°, whereas Lesser, Kranepuhl, and Gad, *Ber.*, 1925, 58, 2109, give m. p. 95—96°), in dry benzene (20 c.c.) was heated with finely powdered phenylurea (4·1 g.; 1 mol.) under reflux during 4 hours; hydrogen chloride was then no longer evolved. The bulky insoluble material was filtered off and digested with a little cold acetone to remove unchanged phenylurea. The colourless residue of s-*3-hydroxy-2-naphthoylphenylurea* crystallised from pyridine–alcohol in needles or long plates (2·7 g.), m. p. 303—305° (decomp.; after shrinking at 275—280°) (Found: N, 9·1. $C_{18}H_{14}O_3N_2$ requires N, 9·15%). It was soluble in warm aqueous potassium hydroxide, giving a bright yellow solution which on the addition of diazotised aniline afforded a red dye.

The benzene filtrate on evaporation yielded a brown transparent resin, which did not contain chlorine and did not exhibit phenolic properties. It dissolved, after long boiling, in aqueous potassium hydroxide, giving a bright yellow solution from which 3-hydroxy-2-naphthoic acid, m. p. and mixed m. p. 216°, was precipitated by mineral acid. The powdered resin, when boiled with aniline, afforded 3-hydroxy-2-naphthanilide, which formed plates from glacial acetic acid, m. p. 244° (cf. Meister Lucius and Brüning, *loc. cit.*).

The following 3-hydroxy-2-naphthoylarylureas were prepared by the same method as that used for the phenyl compound, to which they were similar in properties, and crystallised from pyridine–alcohol: s-*3-hydroxy-2-naphthoyl-*o-*tolylurea*, colourless felted needles, which blackened and shrank at 310° (Found: N, 8·5. $C_{19}H_{16}O_3N_2$ requires N, 8·7%). s-*3-Hydroxy-2-naphthoyl-*p-*tolylurea*, long silky needles, which blackened and shrank at 290° and melted at about 307° (decomp.); yield, 42% (Found: N, 8·6%). s-*3-Hydroxy-2-naphthoyl-*o-*methoxyphenylurea*, cream-coloured needles, which blackened and shrank at 270°; yield, 43% (Found: N, 8·5. $C_{19}H_{16}O_4N_2$ requires N, 8·3%). s-*3-Hydroxy-2-naphthoyl-*p-*methoxyphenylurea*, long, colourless needles, which melted to a yellow liquid when plunged into a bath at 240°; blackening occurred on gradual heating (Found: N, 8·6%). s-*3-Hydroxy-2-naphthoyl-*p-*chlorophenylurea*, pale yellow needles, m. p. 240° (decomp.) (Found: N, 8·0. $C_{18}H_{13}O_3N_2Cl$ requires N, 8·2%).

*3-Hydroxy-2-naphthoylurea.*—A solution of the acid chloride (10 g.; 1 mol.) in dry benzene (40 c.c.) was heated with dry powdered urea (3 g.; 1 mol.) under reflux during 5 hours. The bulky yellow product was separated from the benzene solution (which on evaporation yielded a resin), washed with cold acetone, and digested with cold water. The dried solid crystallised from glacial acetic acid in diamond-shaped plates of *3-hydroxy-2-naphthoylurea*, which charred at 270—275° (Found: N, 12·3. $C_{12}H_{10}O_3N_2$ requires N, 12·1%). The urea dissolved readily in aqueous sodium carbonate, giving a bright yellow solution; when this was heated, ammonia was evolved and sodium 3-hydroxy-2-naphthoate formed.

*Reaction with aniline.* A mixture of 3-hydroxy-2-naphthoylurea (3 g.; 1 mol.) and aniline (1·2 g.; 1 mol.) was heated at 170—180°. Ammonia was evolved and, after 3 hours, the cooled melt was extracted with cold alcohol, which removed unchanged aniline. The residue crystallised from pyridine–alcohol in diamond-shaped plates, m. p. *ca.* 300° (decomp.). The substance was unaffected by cold dilute alkalis and acids, but dissolved in boiling aqueous potassium hydroxide, giving a bright yellow solution from which ammonia was evolved; 3-hydroxy-2-naphthoic acid was precipitated on the addition of acid. The substance appears to be identical with the 2 : 4 diketo-3 : 4-dihydro-ββ-1 : 3-naphthoxazine described by Fries (*loc. cit.*) (Found: C, 67·8; H, 3·6. Calc. for $C_{12}H_7O_3N$: C, 67·6; H, 3·3%).

3-Hydroxy-2-naphthoylurea (1·7 g.) was heated with aniline (7·2 g.), in which it dissolved, at 180° during 1 hour. Ammonia was evolved and needles or long plates soon began to separate. The cooled mass was extracted with boiling alcohol, which was then rapidly filtered. The residue crystallised from pyridine–alcohol in needles, which shrank and blackened at about 280°. It was identical in properties with the *s*-3-hydroxy-2-naphthoylphenylurea described above (Found: N, 9·5. Calc.: N, 9·15%).

The author wishes to express his gratitude to Professor F. S. Kipping, F.R.S., for his kind interest in this work and to Imperial Chemical Industries, Ltd., for a grant.

University College, Nottingham. [*Received, January 15th*, 1938.]

# 84. *Unsaturated Acids of Natural Oils. Part VII. Docosahexaenoic Acid, an Abundant Highly-unsaturated Acid of Cod-liver Oil.*

By ERNEST HAROLD FARMER and FRANTZ AIME VAN DEN HEUVEL.

The $C_{22}$-fraction isolated (in ester form) from the mixed di- and poly-olefinic acids of cod-liver oil by systematic evaporative distillation below 110° in a continuous "molecular" still gives every evidence of being composed of a single, structurally distinct acid. This acid, which displays hexaene unsaturation and yields pure behenic acid on complete hydrogenation, must be regarded as docosahexaenoic acid, $C_{22}H_{32}O_2$. Unlike all previously described polyene acids from fish oils, the acid shows no exaltation of the molecular refraction and hence is entirely unconjugated; moreover, unlike most of the previously isolated polyene acids, it has escaped alteration by heat.

The nature and proportions of the fission products obtained from the hexaene acid by ozonolysis and by oxidation agree with an unconjugated constitution and show definitely that the acid must possess one of five cited formulæ.

THE highly unsaturated acids which occur together with saturated and mono-olefinic forms as glycerides in Japanese sardine oil, cod-liver oil, halibut-liver oil and other fish oils are highly sensitive to heat and below 200° begin to undergo changes which are in part polymerisations but appear to some extent to be isomerisations. As the result of experience gained several years ago by one of us with Dr. F. C. Webb (unpublished work) it became clear that ordinary fractional distillation of the mixtures of more highly unsaturated acids from Japanese sardine oil (even at the lowest pressures at which equilibrium distillation can satisfactorily be carried out, *i.e.*, 0·1—1 mm.) is hopelessly wasteful and inefficient, and the result is not improved by elaborating the routine of fractionation, by increasing the reflux ratio, or by making use of fractionating columns, since these all serve to increase the duration or intensity of heating. It is remarkable how meagre are the yields of the final fractionation products in those cases where the isolation of pure, or substantially pure, polyene acids has been claimed.*

One of the most unsatisfactory features of *all* the specimens of supposedly homogeneous tri- and poly-olefinic acids which have hitherto been isolated from fish oils is the appearance therein of abnormal refractivity: all the specimens show an exaltation of the molecular refraction approximating to 1 unit (see, for example, the values reported by Toyama and Tsuchiya, *Bull. Chem. Soc. Japan*, 1935, **10**, 232, 241, 433, 441, for acids derived from sardine oil; the refractivities observed by Farmer and Webb for sardine oil acids also showed exactly similar exaltations). Presumably the optical anomaly is due to conjugation, and since the original fish oils and their freshly derived acids appear to be entirely free from conjugated chains, as judged by their absorption spectra (Tsujimoto, *Bull. Chem. Soc. Japan*, 1928, **3**, 299; Edisbury, Morton, and Lovern, *Biochem. J.*, 1933, **27**, 1457; see also Morrell, *J. Soc. Chem. Ind.*, 1936, **55**, 101), the conclusion seems justified that the constitutions of the acids have become changed during heating.

In order to overcome the separative difficulties presented by (*a*) the complexity of the mixture of physically similar unsaturated acids in the fish oils and (*b*) the sensitivity of the acids or their esters to heat, we resorted to fractional evaporative ("molecular") distillation of the mixed di- and poly-olefinic acids, the acids being first separated from the accompanying saturated and mono-olefinic forms by fractional crystallisation of the mixed lithium salts prepared from the saponified oils (Tsujimoto's method) and then converted for ease of distillation into their methyl esters. Although the unsaturated ester fraction of each of several fish oils was examined, the present account is concerned only with that obtained from genuine cod-liver oil. Many practical details of the fractionations have been published elsewhere (*J. Soc. Chem. Ind.*, 1938, **57**, 24) together with comparisons of the products with those isolated by other workers; it is sufficient, however, here to state that sharp separation of the mixed acids (as their esters) from the cod-liver

* The supposedly pure clupanodonic acid ($C_{22}H_{34}O_2$) isolated by Toyama and Tsuchiya (*loc. cit.*, p. 433) from Japanese sardine oil amounted to less than 5 g. from 10 kg. of oil. Other yields of polyene acids reported in the literature are comparable.

oil into fractions consisting respectively of $C_{16}$-, $C_{18}$-, $C_{20}$-, $C_{22}$- and higher acids was accomplished, and of these only one, the $C_{22}$-fraction, appeared to be homogeneous as regards the degree of unsaturation of its material. The $C_{22}$-fraction was the most abundant of the series of fractions, and we regard it on the evidence discussed below as composed of a structurally homogeneous (but not necessarily geometrically homogeneous) compound.

The methyl ester of the $C_{22}$-acid consistently gave hydrogenation values corresponding exactly with hexaene unsaturation, and the reduced acid therefrom agreed immediately (*i.e.*, without recrystallisation) in melting point and *X*-ray diagram with behenic acid of a degree of purity greater than 99%. The oxidation results also are entirely consistent with the possession by the acid of a high degree of structural homogeneity. Thus the evidence leaves little doubt but that one of the chief highly unsaturated acids of cod-liver oil is docosahexaenoic acid, $C_{22}H_{32}O_2$, and it is to be noted that no *pentaene* $C_{22}$-acid identifiable with Tsujimoto's clupanodonic acid from Japanese sardine oil * is present as an original constituent in cod-liver oil.

On ozonolysis the methyl ester gave immediately acetaldehyde (uncontaminated with formic acid) and carbon dioxide, and the residues on further oxidation with hydrogen peroxide gave succinic acid, crystalline methyl hydrogen succinate, and some acetic acid; no oxalic acid, or dibasic acid other than succinic acid, was formed. The total absence of formaldehyde or formic acid, and of fatty aldehydes or acids higher than acetaldehyde or acetic acid, showed that one of the end groups of the polyene acid must be $CH_3{\cdot}CH⁚$; and the production of methyl hydrogen succinate showed the other end group to be $⁚CH{\cdot}[CH_2]_2{\cdot}CO_2H$. Estimation of the proportion of acetic acid and succinic acid formed by complete oxidation of the *free* polyene acid gave the values 4·8 mols. and 1·3 mols. respectively; the proportion of carbon dioxide formed was through oversight not accurately measured, but it was observed to be in excess of 2·7 mols. (see p. 430).

In view of the large proportions of acetic acid and carbon dioxide thus formed and the absence of oxalic acid, it follows that a large proportion of the polyene acid was built up by repetition of the same group, $⁚CH{\cdot}CH_2{\cdot}CH⁚$, which characterises linoleic and linolenic acid: this conclusion, moreover, agrees with the fact that docosahexaenoic acid as now obtained by us, unlike the previously isolated polyene acids from fish oils referred to above, showed *no* exaltation of the molecular refraction. The molecule of *free* succinic acid formed (as distinct from the half ester) must of course be derived from a non-terminal $⁚CH{\cdot}[CH_2]_2{\cdot}CH⁚$ group.

The formula for docosahexaenoic acid must then contain four $⁚CH{\cdot}CH_2{\cdot}CH⁚$ groups, and these can be arranged between the above-mentioned terminal groups and in relation to the single group $⁚CH{\cdot}[CH_2]_2{\cdot}$ in five ways, shown in the formulæ (I)—(V):

(I) $CHMe[⁚CH{\cdot}CH_2{\cdot}CH]_4⁚CH{\cdot}[CH_2]_2{\cdot}CH⁚CH{\cdot}[CH_2]_2{\cdot}CO_2H$
(II) $CHMe[⁚CH{\cdot}CH_2{\cdot}CH]_3⁚CH{\cdot}[CH_2]_2{\cdot}CH⁚CH{\cdot}CH_2{\cdot}CH⁚CH{\cdot}[CH_2]_2{\cdot}CO_2H$
(III) $CHMe[⁚CH{\cdot}CH_2{\cdot}CH]_2⁚CH{\cdot}[CH_2]_2{\cdot}CH[⁚CH{\cdot}CH_2{\cdot}CH]_2⁚CH{\cdot}[CH_2]_2{\cdot}CO_2H$
(IV) $CHMe⁚CH{\cdot}CH_2{\cdot}CH⁚CH{\cdot}[CH_2]_2{\cdot}CH[⁚CH{\cdot}CH_2{\cdot}CH]_3⁚CH{\cdot}[CH_2]_2{\cdot}CO_2H$
(V) $CHMe⁚CH{\cdot}[CH_2]_2{\cdot}CH[⁚CH{\cdot}CH_2{\cdot}CH]_4⁚CH{\cdot}[CH_2]_2{\cdot}CO_2H$

Docosahexaenoic acid possesses one of these formulæ, but a decision between the five must await detailed examination of the constitution of the partial addition products of the hexaene acid.

As mentioned above, docosahexaenoic acid was observed by Toyama and Tsuchiya (*loc. cit.*, pp. 433, 539) and by Farmer and Webb to accompany clupanodonic acid in sardine oil, but neither group of workers isolated it in pure condition. The hexaene acid is with little doubt an original constituent of sardine oil and is probably identical with that which we have found to be an important constituent of cod-liver oil. The clupanodonic acid, on the other hand, we believe to be a secondarily formed product, probably derived from docosahexaenoic acid by the action of heat; for in fractional distillations which we have carried out on Japanese sardine oil esters (" molecular " still), no less than in those we have conducted on cod-liver oil esters, we have failed to recognise a pentaene $C_{22}$-fraction.

* Clupanodonic acid was first isolated from Japanese sardine oil by Tsujimoto. Later, Toyama and Tsuchiya (*loc. cit.*) and simultaneously Farmer and Webb observed that this pentaene $C_{22}$-acid was accompanied by a hexaene $C_{22}$-acid.

## EXPERIMENTAL.

*Isolation of Di- and Poly-ene Acids from Cod-liver Oil.*—The freshly derived oil (6 kg.) from selected cod livers was diluted with methylated spirit (4 l.) and heated to 60°. To this solution an excess of 50% aqueous sodium hydroxide solution (1000 g. of sodium hydroxide) at 60° was added little by little with stirring. The mixture was simmered and stirred for 45 minutes, then cooled, and strongly acidified with 15% hydrochloric acid. The lower aqueous layer was syphoned off, the oily layer, consisting of free acids, washed successively with 15% hydrochloric acid (3 times) and with hot water (4 times), and then taken up in acetone (4 l.), and the solution dried overnight with calcium chloride (1 lb.).

The filtered acetone solution of free acids was further diluted with acetone (15 l.) and then treated at 50° very gradually (with stirring) with a slight excess of saturated aqueous lithium hydroxide solution (440 g. of lithium hydroxide in 3·2 l. of water) warmed to 50°. The alkaline acetone solution of lithium salts was simmered for 20 minutes and then diluted with acetone (about 45 l. necessary) until the total of the solvents added represented a mixture containing 95% of acetone and 5% of water. On standing overnight, the solution deposited a precipitate consisting of the bulk of the salts of the saturated and mono-olefinic acids. The precipitate was removed by centrifuging, and the filtrate freed from acetone by distillation: a solution of the lithium salts of the di- and poly-ene acids remained, and this was first freed from the unsaponifiable matter of the oil by thorough extraction with ether and then acidified with 15% hydrochloric acid. The mixture of free unsaturated acids was extracted with ether, and the ethereal solution washed with water, dried over sodium sulphate, and evaporated.

The di- and poly-ene acids were esterified by refluxing them for 3 hours with 8 times their volume of 4% methyl-alcoholic hydrogen chloride. A part (60%) of the alcohol was distilled from the product, and the residual material treated with ice. Two layers separated, of which the upper was separated, washed well with water and with sodium carbonate, and then taken up in ether. The well-dried (sodium sulphate) ethereal solution gave the mixed unsaturated acids as a rather thick oil. Yield, 1200 g.

*The Unsaponifiable Matter.*—The oily neutral material extracted from the lithium salts with ether deposited (i) a solid, crystallising in prisms, m. p. 148°, and forming with acetic anhydride an acetate, m. p. 113°, (ii) a very small amount of an amorphous solid, insoluble in most organic solvents, and (iii) a highly unsaturated, orange-yellow oil, b. p. 160—173°/0·5 mm. The crystalline product (i) gave the reactions of a sterol and agreed in m. p. and mixed m. p. with cholesterol * (cholesterol acetate melts at 115°); the other products have not been investigated.

*The $C_{22}$-fraction of Unsaturated Acids.*—Evaporative distillation of the mixed unsaturated acids in the form of their methyl esters at about $10^{-4}$ mm. pressure was conducted in a continuous "molecular" still by a technique which will be described elsewhere. The highest temperature employed was 110° and the total time of contact with the heated surface was about 60 secs. The fraction containing only the ester(s) of $C_{22}$-acid(s) amounted to 225 g., but a further small quantity was present in the lower and the higher connecting fractions; this fraction had $n_D^{20°}$ 1·49300, $[R_L]_D$ 107·25, hydrogen value 356 (Calc. for $C_{23}H_{34}O_2|_6^{=}$: $[R_L]_D$ 107·2; hydrogen value 353·5).

No departure from hexaene unsaturation was observed when this fraction was afterwards divided into two portions by a further evaporative distillation; moreover, the ester gave *at once* on hydrogenation and evaporation of the solvent a saturated ester, m. p. 53°. This ester was in every way identical with pure methyl behenate (m. p. 54°) and the acid derived therefrom by saponification (m. p. 82°) was found to be behenic acid (m. p. 82°, mixed m. p. 82°). We are indebted to Dr. S. H. Piper for examining the *X*-ray spacing of this acid, and to Professor A. C. Chibnall for comparing the acid directly with synthetic behenic acid: from the results of these observations the acid is estimated to have a degree of purity exceeding 99%.

*Oxidation of Methyl Docosahexaenoate.*—The ester (5 g.) was dissolved in acetone (300 c.c.), the solution placed in a flask surmounted by a percolator containing an excess of powdered potassium permanganate, and the percolator fitted with a reflux condenser. The solvent was refluxed until the colour of permanganate in the reaction flask remained just permanent, the residual colour being then discharged by addition of a drop of perhydrol. The manganese mud and admixed salts were filtered off, dried, and thoroughly extracted with boiling water; the filtrate was distilled until only 20 c.c. of liquid remained in the flask. To this liquid residue

* A beautifully crystalline hydrocarbon (fine needles, m. p. 76°) appeared in the unsaponifiable matter isolated by Dr. Webb from Japanese sardine oil. This has now been definitely identified as cholesterilene (Found: C, 88·0; H, 12·05. Calc. for $C_{27}H_{44}$: C, 87·95; H, 12·05%), doubtless formed from cholesterol by the action of alcoholic hydrogen chloride, followed by distillation.

a few drops of 10% sodium carbonate solution were added, the product combined with the aqueous extract of the manganese mud, and the whole evaporated to dryness. The solid residue (A) was dissolved in excess of 25% sulphuric acid, and the solution distilled into a solution of sodium carbonate (with addition of more water to the flask at intervals) until no more acid passed over. The alkaline solution of the distillate was evaporated to dryness, and the residue acidified and thoroughly extracted with ether. The extract was dried, and the ether cautiously distilled under an efficient column. The acidic residue was distilled under a short column to free it from ether, and only a minute tarry residue remained in the flask. An aliquot portion of the distillate was neutralised with sodium carbonate, and the salt so formed converted into its *p*-bromophenacyl ester. This melted at once at 84° and on recrystallisation at 85°; it did not depress the m. p. (85°) of authentic *p*-bromophenacyl acetate. Formic acid was thus absent and any higher-boiling fatty acid contained in the small tarry distillate was entirely negligible in amount. Fractional distillation of the remainder of the (aqueous) acid distillate gave as the last fraction nearly anhydrous acetic acid, b. p. 114—116° (Found: *M*, monobasic, 59·7. Calc., 60·0). The unused fractions of acetic acid were united and diluted to a known volume, and aliquot parts of the solution titrated. The total yield of acetic acid estimated in this way was 3·13 g., *i.e.*, 1 mol. of ester yielded at least 4 mols. of acetic acid.

The aqueous liquid remaining after the volatile acids had been distilled off yielded on exhaustive continuous extraction with ether a crystalline acid, m. p. 178—184°. This was succinic acid and, when freed from a trace of oily matter, melted at 184° (mixed m p. 184°).

To determine more accurately the proportions of acetic acid and succinic acid produced by oxidation, a further 3·42 g. (0·01 g.-mol.) of ester were oxidised with potassium permanganate in acetone as above. The solid residue (A) (see above) was dissolved in water and made up to 100 c.c.; then the acetic acid liberated by sulphuric acid from an aliquot part of this solution was estimated by a standard steam distillation–titration method. The succinic acid from the remainder of the solution of potassium salts was isolated as above, recrystallised, and weighed. Total yield of acetic acid, 3·42 g. (4·87 mols.); total yield of succinic acid, 1·75 g. (1·30 mols.).

*Ozonolysis of Methyl Docosahexaenoate.*—The ester (4 g.) was ozonised in chloroform (20 c.c.) at 0—5°. The ozonide, when freed from solvent, was a colourless thick syrup. This was decomposed by gradual warming with water to 90°, the volatile decomposition products being swept by a stream of hydrogen through a train of five wash-bottles containing dimedon reagent (2 bottles) and freshly prepared 5N-baryta (3 bottles). The combined contents of the first two bottles, when treated with a drop of acetic acid and warmed slightly, yielded a copious precipitate which melted *at once* at 138—139°. This was the dimedon derivative of acetaldehyde (mixed m. p. with authentic specimen, 138—139°). Thus the volatile aldehydic product was free from formaldehyde.

The production of carbon dioxide from the ozonide began in the cold and continued briskly when the reaction flask was warmed. From the amount of barium carbonate formed in the last three wash-bottles, the amount of carbon dioxide passing through the latter was computed to be 2·7 mols. A proportion, however, of the carbon dioxide had been absorbed in the dimedon reagent, which contained sodium carbonate solution.*

The aqueous liquid remaining in the decomposition flask contained a yellowish oil, which was separated by decantation of the aqueous layer. This oil was taken up in ether, and the ethereal solution dried and evaporated. Yield of oil, 1 g. The aqueous liquid, when extracted thoroughly with ether and the solution dried and cautiously distilled (column), yielded a liquid residue. This was repeatedly extracted with light petroleum, the undissolved yellow oil combined with the preceding oily product, and the petroleum extract evaporated. From the petroleum extract acetic acid (*p*-bromophenacyl ester, m. p. 84°) was obtained, which after distillation was estimated by titration. Yield, 3·1 mols. The yellow oil was treated overnight with dilute perhydrol, then taken up in ether, and the solution (after drying) allowed to evaporate slowly. A portion of the oil solidified, yielding crystals of methyl hydrogen succinate, m. p. 57°, which on hydrolysis gave succinic acid; the remainder of the oil was directly hydrolysed, yielding a further quantity of succinic acid.

Continuous extraction of the aqueous portion of the decomposition product with ether gave succinic acid in an amount corresponding to 0·46 mol.

We thank the Royal Society for a grant to one of us (E. H. F.).

Imperial College, London, S.W. 7. [*Received, February 8th*, 1938.]

* Through an oversight the complete yield of carbon dioxide was not determined.

## 85. *The Configurations of the Isomeric Diazocyanides, and Some Measurements of their Rates of Interconversion.*

By R. J. W. Le Fèvre and H. Vine.

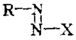
Measurements of the dipole moments of several pairs of isomeric diazocyanides have provided definite physical evidence for the correctness of the configurations allotted to these compounds by Hantzsch, *viz.*, that the *cis*-isomerides are the less stable and are those primarily produced.* The spontaneous isomerisation which they undergo in benzene solution has been followed by means of the dielectric constant. The *trans*-isomerides are produced at rates obeying the unimolecular law, and in one case measurements at two temperatures have afforded a value of the activation energy. The measured rates of isomerisation of the substituted diazobenzenecyanides examined were in the order

$$\left.\begin{matrix}p\text{-chloro-}\\ p\text{-bromo-}\end{matrix}\right\} > \left.\begin{matrix}p\text{-nitro-}\\ o\text{-bromo-}\end{matrix}\right\} > 2:4:6\text{-tribromo-}$$

That the majority of aromatic diazo-compounds are electrovalent salts of the type $RN_2^+X^-$ (halides, sulphates, nitrates, etc.) was clearly shown by Hantzsch's work on the conductivity of their solutions. They are water-soluble and generally colourless, and were regarded as salts of the corresponding diazonium hydroxides, $RN_2^+OH^-$. The diazonium sulphites ($RN_2^+SO_3H^-$), cyanides ($RN_2^+CN^-$) and the hydroxides themselves, however, except in very dilute solution or in the presence of acid, pass to a large extent into the covalent diazo-sulphonic acids ($R{\cdot}N{:}N{\cdot}SO_3H$), -cyanides ($R{\cdot}N{:}N{\cdot}CN$), and -hydroxides ($R{\cdot}N{:}N{\cdot}OH$), the normal diazohydroxides and sulphonic acids being capable of isolation only in the form of their metallic derivatives.

In all three cases the covalent diazo-compounds first obtained underwent transformation into more stable isomers, and Hantzsch regarded the two forms as *cis*- and *trans*-isomerides, as (I) and (II). His views on the isomeric diazotates were only generally

(I.) *cis*-.



(II.) *trans*-.

accepted after a long controversy (1894—1902), in the course of which the discovery of similar isomerism amongst the diazo-sulphonates and -cyanides was of great importance.

The diazonium cyanides could not be isolated except as double salts with silver cyanide, of the general formula $RN_2{\cdot}Ag(CN)_2$, or in one instance, that of the *p*-anisole derivative, which showed the greatest tendency to ionise, as a crystalline salt of the formula

$$CH_3{\cdot}O{\cdot}C_6H_4{\cdot}N_2{\cdot}CN,HCN,2H_2O.$$

The isomeric diazocyanides were both coloured, low-melting solids, readily soluble in organic solvents but sparingly so in water. The labile normal cyanide always had the greater solubility and lower melting point, and in alcoholic solution it coupled much the more rapidly with β-naphthol. The transformation of the normal into the *iso*-diazocyanides proceeded spontaneously in solution in organic solvents at the ordinary temperature, but less rapidly than the transformation of the diazosulphonates; the diazotates generally only changed at an appreciable rate when heated.

*Configurations of the Isomerides.*—Hantzsch argued by analogy with the isomerism of ethylenic compounds and recognised the less stable forms of the diazotates, cyanides, and sulphonates as *cis* (*syn*) and the more stable forms as *trans* (*anti*). He considered this conclusion to be strongly supported by the fact that the labile cyanides decomposed readily in contact with copper powder, with the liberation of nitrogen and the formation of nitriles, whereas the stable forms did not, it being supposed that this elimination would occur more readily when the groups R and CN were nearer together. The fallacy of reasoning of this

* A summary of the experimental work of Hantzsch and his collaborators is given in " Die Diazoverbindungen," by Hantzsch and Reddelien, 1921.

type is illustrated by the greater stability of *cis*- than of *trans*-dichloroethylene (Ebert a Büll, *Z. physikal. Chem.*, 1931, *A*, **152**, 451), and by the incorrectness of the oxime co figurations derived from a consideration of the Beckmann change and dehydration reactior

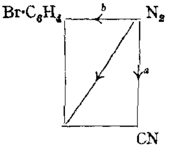
*The present work was undertaken because dipole-moment measurements afford a mea of determining the configuration of geometrical isomerides independently of argumen from analogy. The results now recorded thus provide the first certain confirmation of th correctness of Hantzsch's allocations. The moments of the substances are given in th following table:*

| Diazobenzenecyanide derivative. | Dipole moment (D.).* (*cis*-), labile. | (*trans*-), stable. |
|---|---|---|
| 4-Chloro- | 2·93 | 3·73 |
| 4-Bromo- | 2·91 | 3·78 |
| 4-Nitro- | 2·04 | 1·47 |
| 2-Bromo- | 3·79 | 5·32 |
| 2 : 4 : 6-Tribromo- | 2·5 | 4·0 |

* All moments given subsequently are in Debye units (e.s.u. × $10^{-18}$).

These values may be considered in relation to rough vector diagrams of the type giver below.

When the measurements on the 4-bromo-derivatives were first reported (*Chem. and Ind.* 1937, **56**, 680), it was supposed that the moments *a* and *b* associated with the group $N_2$—CN and *p*-Br—$C_6H_4$—$N_2$ would both be directed *away* from the azo-group, as in (III



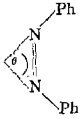
Resultant > *a*.

(III.)

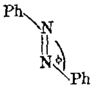
$$\mathrm{Br{\cdot}C_6H_4} \overset{b}{\longleftarrow} \mathrm{N_2} \overset{a}{\longrightarrow} \mathrm{CN}$$

Resultant = *a* − *b*

(IV.)



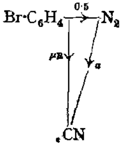
(V.)



(VI.)

and (IV). In these circumstances the greater moment would be that of the *cis*-isomer However, such a conclusion became doubtful when the moment of *cis*-azobenzene was foun to be 3·0 (unpublished work), from which the value of the $C_6H_5 \rightarrow N_2$ link moment coul be estimated, by making a reasonable assumption regarding the angle θ (in V).

The crystal analysis of *trans*-azobenzene (Robertson, Prasad, and Woodward, *Proc Roy. Soc.*, 1936, *A*, **154**, 187) has not yet been completely performed, but from the isomorphism with *trans*-stilbene it can be concluded that these molecules are similar in that φ is probably *ca.* 130° (VI), and so if (VI) ⟶ (V) merely by rotation about the N = N axis, θ becomes 80°. For such a configuration, since $2\mu\cos\frac{1}{2}\theta = 3{\cdot}0$, the $C_6H_5 \rightarrow N_2$ link moment is *ca.* 2·0. The $C_6H_5 \rightarrow$ Hal. moment being *ca.* 1·5, it now appears that the resultant of the *p*-Hal.-$C_6H_4$-$N_2$ group will be *ca.* 0·5, directed *towards* the azo-group. The moment associated with the CN group itself (*ca.* 4·0) will be considerably greater than any opposing $N_2 \leftarrow$CN moment, and the resultant will be directed *away* from the azo-group.



(VII.)

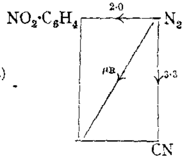
$\mu_B < a$.

$$\mathrm{Br{\cdot}C_6H_4} \overset{0\cdot5}{\longrightarrow} \mathrm{N_2} \overset{a}{\longrightarrow} \mathrm{CN}$$

(VIII.) $\mu_B \simeq a + 0{\cdot}5$; hence $a \simeq 3{\cdot}3$.

Therefore, as shown in (VII) and (VIII), for *trans-p*-chloro- or -bromo-benzenediazocyanide, $\mu_R \simeq a + 0{\cdot}5$, and for the *cis*-form $\mu_R$ will be slightly less than *a*. Since the moment of the stable form is greater by nearly 1 than that of the labile form, the result is in agreement with Hantzsch's configurations. This conclusion is confirmed by the moments of the *p*-nitro-derivatives, for here the $R \rightarrow NO_2$ moment is *ca.* 4·0, and the resultant of the $p\text{-}NO_2{\cdot}C_6H_4\text{—}N_2$ group is *ca.* 2·0, directed *away* from the azo-group. The moment of the *cis*-form should therefore be greater than that of the *trans*-, as shown in (IX) and (X); experimentally, the labile and the stable form are found to have moments of 2·05 and 1·47 respectively.

(IX.)




$$NO_2{\cdot}C_6H_4 \overset{2\cdot0}{\longleftarrow} N_2 \overset{3\cdot3}{\longrightarrow} CN$$
$$\mu_R \simeq 3{\cdot}3 - 2{\cdot}0.$$
(X.)

The moments of the 2 : 4 : 6-tribromo-derivatives are also in agreement with this scheme, for the moment of the $C_6H_2Br_3\text{—}N_2$ group should be very approximately that of $C_6H_5\text{—}N_2$, *i.e.*, *ca.* 2·0, directed *towards* the azo-group, and the *trans*- (stable) form consequently should have a higher moment than its isomer. Since the aromatic nucleus in 2-bromobenzenediazocyanide is not symmetrical, problems of rotation arise, and the moments of this or its derivatives cannot well be predicted.

It should be emphasised that the conclusiveness of this argument lies in the reversal of the difference between the moments of the isomers when proceeding from the *p*-halogeno- and 2 : 4 : 6-tribromo-derivatives to the *p*-nitro-derivative.

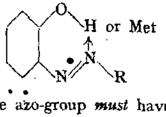
Previous physical measurements on the diazocyanides have not provided any definite evidence on the point in question. Stewart (J., 1907, **91**, 199) suggested that, of two geometrical isomerides, the more symmetrical showed the greater power of absorbing light, and that this property might be used in the determination of molecular structure. No such generalisation can be applied to the azo- and diazo-compounds, for although in 2 : 4 : 6-tribromobenzenediazocyanide the *trans*- (stable) form has the greater absorption in both the visible and the near ultra-violet region (Hantzsch and Lifschitz, *Ber.*, 1912, **45**, 3011), yet in potassium 2-chlorobenzenediazosulphonate (Hantzsch and Lifschitz, *loc. cit.*), and 4-bromobenzenediazocyanide as well as azobenzene (present work), the stable form absorbs more in the ultra-violet but less in the visible than the labile isomer.

Brühl (*Ber.*, 1896, **29**, 2907) found that normal and *iso*-2 : 4-dibromobenzenediazocyanide had molecular refractions for the $Na_D$ line of 56·59 and 58·64 respectively in benzene solution, which were in accordance with the geueral observation that the *trans*-isomer of a given pair had the greater molecular refraction. Measurement of the molecular refraction of several pairs of diazocyanides has been incidental to the determination of their dipole moments, and the *trans*- (stable) isomers have the higher value in each case, thus :

| Diazobenzenecyanide derivative. | $[R_L]_D$. *cis*-. | $[R_L]_D$. *trans*-. |
|---|---|---|
| 4-Chloro- | 46·1 | 48·0 |
| 4-Bromo- | 49·9 | 52·3 |
| 4-Nitro- | 44·7 | 48·6 |

| Diazobenzenecyanide derivative. | $[R_L]_D$. *cis*-. | $[R_L]_D$. *trans*-. |
|---|---|---|
| 2-Bromo- | 47·2 | 51·6 |
| 2 : 4 : 6-Tribromo- | 64 | 68 |

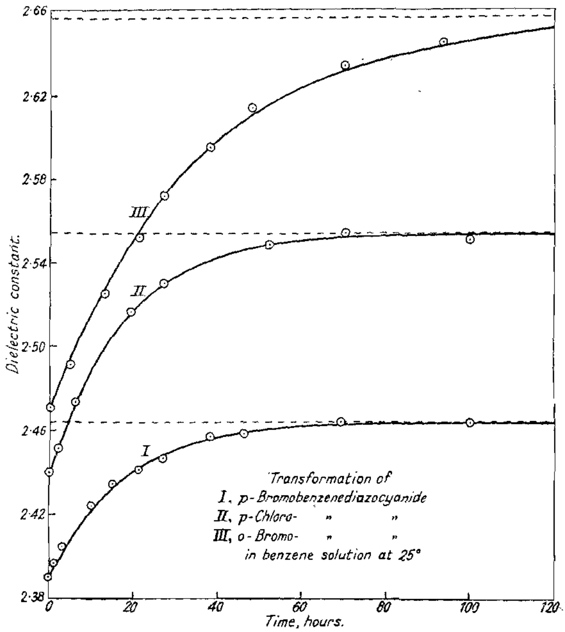
It seems probable that among azo-compounds the *trans*- form is always the more stable, for in addition to the results now recorded, Bergmann, Engel, and Sándor (*Ber.*, 1930, **63**, 2572) have reported a zero moment for azobenzene. This, in view of the fact that no tendency to pass into a more stable form had been observed, was evidence for the greater stability of the *trans*-configuration of the azo-group in this molecule. Such a view is in harmony with the formulation of the *o*-hydroxyazo-mordant dyes as chelated compounds in which the azo-group *must* have



a *trans*-structure (Pfeiffer, *J. pr. Chem.*, 1930, **126**, 108; Sidgwick, "The Electronic Theory of Valency," p. 234), and also with the recent discovery of a second, less stable, form of azobenzene, produced by the action of light (Hartley, *Nature*, 1937, **140**, 281) and shown by its moment to be the *cis*-isomer.

*Rates of Isomerisation.*—The transformation of the *cis*- into the *trans*-diazocyanides in pure benzene solution has been followed by dielectric-constant measurements. The solutions were kept in brown glass bottles, although ordinary daylight does not have much effect at the concentrations used (1—5%). The change goes to completion, following the

FIG. 1.




unimolecular law, and Fig. 1 shows the transformation of the *p*-chloro-, *p*-bromo-, and *o*-bromo-diazocyanides at 25°. The broken lines show the final values obtained. The curves have been calculated from the equation $dx/dt = k(a - x)$, the best values of $k$ being chosen. The transformation of *p*-nitrobenzenediazocyanide is shown in Fig. 2, but in this case the change in dielectric constant is smaller and the experimental error is therefore increased. Fig. 3 shows the transformation of *p*-bromobenzenediazocyanide at 57·5°, at which temperature a rough measurement of the rate of change of 2 : 4 : 6-tribromobenzenediazocyanide (which does not invert at an appreciable rate at 25°) has also been made. The velocity constants are summarised on p. 435 :

| Diazobenzenecyanide derivative. | $k_{25^\circ}$, hr.$^{-1}$. | $k_{57\cdot5^\circ}$, hr.$^{-1}$. | Diazobenzenecyanide derivative. | $k_{25^\circ}$, hr.$^{-1}$. | $k_{57\cdot5^\circ}$, hr.$^{-1}$. |
|---|---|---|---|---|---|
| 4-Chloro- .................. | 0·058 | — | 2-Bromo- .................. | 0·028 | — |
| 4-Bromo- .................. | 0·058 | 2·08 | 2 : 4 : 6-Tribromo- ...... | — | 0·11 |
| 4-Nitro- .................... | 0·026 | — | | | |

Within the limits of experimental error, identical values have been found for the *p*-bromo-compound at 25° and 55° by Dr. G. S. Hartley, using a photometric method in which solu-

FIG. 2.

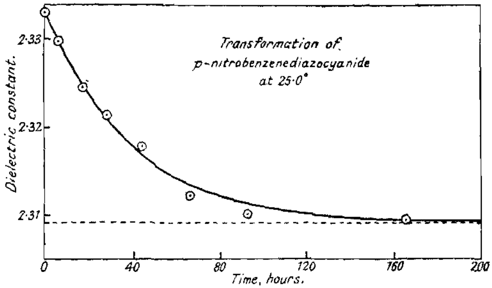
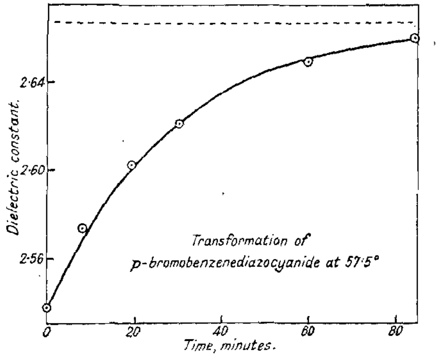



FIG. 3.




tions of much greater dilution than ours are used. From the dielectric-constant measurements at two temperatures on the *p*-bromo-derivative, since $\log_e k_2/k_1 = E(T_2 - T_1)/\boldsymbol{R}$, the energy of activation is 21·6 kg.-cals. (Hartley finds 22·0 kg.-cals.). The transformation of *cis*- into *trans*-azobenzene has a similar activation energy (23·0 kg.-cals., Hartley), and it is therefore probable that the transformation in this case and in the diazocyanides occurs by the same mechanism.

The effect of substituents in the benzene ring is of interest. Hantzsch and Danziger (*Ber.*, 1897, **30**, 2529) concluded that, in general, halogen atoms in the para- and more

especially the ortho-positions reduced the readiness of transformation and increased the stability of the *cis*-diazocyanides, whilst alkyl or methoxy-groups had the opposite effect. They made purely qualitative observations of the behaviour of the *cis*-cyanides in the solid state or when dissolved in alcohol and reprecipitated with water. Those substances which have been investigated in the present work were tabulated by them as follows:

| Derivative. | | |
|---|---|---|
| 4-Nitro- | Unstable | Very easily isomerisable |
| 4-Chloro- | More stable | Easily isomerisable |
| 4-Bromo- | Stable | Fairly easily isomerisable |
| 2-Bromo- | Very stable | Difficultly isomerisable |
| 2 : 4 : 6-Tribromo- | Very stable | Difficultly isomerisable |

We have found, however, that the rates of change of the *p*-chloro- and the *p*-bromo-cyanide in benzene solution at the same temperature are equal, whereas that of the *p*-nitro-cyanide is less. The transformation of the *o*-bromo- is half as fast as that of the *p*-bromo-cyanide, and that of the 2 : 4 : 6-tribromo-derivative is reduced to one-twentieth. The influence of substituents in the *p*-position is in the same order as their permanent electron-attracting effect.

It is probable that the thermal transformation takes place only very slowly in the solid but more rapidly in the fused state. Therefore in those cases where the production of small amounts of *trans*- can depress the m. p. of the *cis*-form below room temperature, the initially slow isomerisation could proceed more rapidly in the melt. Since both *cis*-*p*-chloro- and -*p*-nitro-benzenediazocyanides have lower m. p.'s (28—30°) than that of *cis*-*p*-bromobenzenediazocyanide (42—43°), this suggestion may account for Hantzsch and Danziger's observation that the former underwent transformation more readily than the latter. We noticed that a sample of *cis*-*p*-chlorobenzenediazocyanide left in a desiccator at *ca.* 23° for a few hours became partly liquid, and then resolidified on mixing. On the other hand, a pure dry sample of the *p*-bromo-derivative could be kept unchanged at 0° for two months.

However, transformation can occur under the action of light in both the solid and the dissolved state. For instance, Ciusa (*Atti R. Accad. Lincei*, 1906, **15**, II, 137) observed that isomerisation of *cis*-2 : 4 : 6-tribromobenzenediazocyanide was brought about in benzene solution by sunlight, and Hartley has shown the effect to be reversible in both azo-compounds and diazocyanides. We found that solid *cis*-tribromobenzenediazocyanide, when exposed to the spectrum of a mercury-vapour lamp, also became reddened on the surface by the chief mercury lines between wave-lengths 3000 to 4500 A.

## EXPERIMENTAL.

*Preparation of Materials.*—*p*-Chloro-, *o*- and *p*-bromo-, and *p*-nitro-benzenedizaocyanides were prepared by the following modification of the recorded procedures (Hantzsch and Schultze, *Ber.*, 1895, **28**, 666; Hantzsch and Danziger, *loc. cit.*). The appropriate base (0·1 g.-mol.) was dissolved in concentrated hydrochloric acid (45 c.c., 0·45 g.-mol.) and water (45 c.c.) and treated with sodium nitrite (0·1 g.-mol.). The diazotised solution was filtered and cooled to —10° in solid carbon dioxide–alcohol, 50 c.c. of absolute alcohol being added in order to prevent the mixture freezing. Potassium cyanide (*ca.* 13 g., 0·2 g.-mol.) in 25 c.c. of water was added slowly, the mixture being well stirred. The final mixture thus remained acid to litmus. The orange-coloured precipitate was filtered off, washed with ice-cold water, and spread on a porous plate. It was then dissolved in light petroleum with a little ether, dried over anhydrous sodium sulphate, and well cooled in solid carbon dioxide–alcohol. The pure labile diazocyanides were thus obtained as small orange-coloured needles or plates, which were readily dried on a porous tile.

The stable diazocyanides were obtained by evaporation of the solutions used in the measurement of the dipole moments and the velocity of transformation of the labile isomers, and were recrystallised in a similar manner from ether and light petroleum by cooling strongly. They were very similar in appearance to their isomers, but somewhat redder. They crystallised in needles, and slow evaporation of *trans*-*p*-chlorobenzenediazocyanide solution produced crystals up to 4 cm. in length.

2 : 4 : 6-Tribromoaniline, being a very weak base, could not be treated in the above manner. The pure diazonium sulphate was obtained by the addition of amyl nitrite to the amine dissolved

TABLE I.

| $w_1$. | $\epsilon^{25°}_{1200}$. | $d^{25°}_{4°}$. | $\alpha\epsilon_2$. | $\beta$. | $n^{25°}_D$. | $r_{12}$. | $[R_L]_D$. |
|---|---|---|---|---|---|---|---|
| 0 | 2·2725 | 0·87378 | — | — | 1·49725 | 0·33503 | — |
| | | | *p-Chlorobenzenediazocyanide.* | | | | |
| | | | Labile form (*cis*-). | | | | |
| 0·01629 | 2·3708 | 0·87839 | 6·03 | 0·324 | 1·49866 | 0·33408 | 45·8 |
| 0·03023 | 2·4531 | 0·88234 | 5·97 | 0·324 | 1·50003 | 0·33335 | 46·2 |
| 0·03865 | 2·5005 | 0·88478 | 5·90 | 0·326 | 1·50076 | 0·33285 | 46·1 |
| | | | Stable form (*trans*-). | | | | |
| 0·00592 | 2·3285 | 0·87537 | 9·46 | 0·308 | 1·49794 | 0·33482 | 49·5 |
| 0·00692 | 2·3386 | 0·87571 | 9·55 | 0·319 | 1·49798 | 0·33471 | 47·8 |
| 0·01098 | 2·3771 | 0·87690 | 9·53 | 0·325 | 1·49848 | 0·33453 | 47·8 |
| 0·01154 | 2·3824 | 0·87703 | 9·52 | 0·322 | 1·49854 | 0·33453 | 48·3 |
| | | | *p-Bromobenzenediazocyanide.* | | | | |
| | | | Labile form (*cis*-). | | | | |
| 0·00746 | 2·3084 | 0·87675 | 4·81 | 0·456 | 1·49795 | 0·33430 | 49·8 |
| 0·00879 | 2·3138 | 0·87729 | 4·70 | 0·457 | 1·49811 | 0·33418 | 50·0 |
| 0·01220 | 2·3301 | 0·87867 | 4·72 | 0·459 | 1·49844 | 0·33384 | 49·0 |
| | | | Stable form (*trans*-). | | | | |
| 0·00595 | 2·3186 | 0·87605 | 7·75 | 0·437 | 1·49788 | 0·33452 | 52·4 |
| 0·00766 | 2·3329 | 0·87678 | 7·88 | 0·448 | 1·49810 | 0·33437 | 52·3 |
| 0·01058 | 2·3548 | 0·87790 | 7·78 | 0·446 | 1·49840 | 0·33411 | 52·1 |
| | | | *p-Nitrobenzenediazocyanide.* | | | | |
| | | | Labile form (*cis*-). | | | | |
| 0·01667 | 2·3218 | 0·87920 | 2·96 | 0·372 | 1·49855 | 0·33371 | 45·0 |
| 0·01960 | 2·3286 | 0·88010 | 2·86 | 0·369 | 1·49866 | 0·33343 | 44·6 |
| 0·02037 | 2·3275 | 0·88032 | 2·70 | 0·367 | 1·49868 | 0·33335 | 44·4 |
| 0·02060 | 2·3329 | 0·88042 | 2·93 | 0·369 | — | — | — |
| | | | Stable form (*trans*-). | | | | |
| 0·00880 | 2·2872 | 0·87654 | 1·67 | 0·359 | 1·49824 | 0·33454 | 49·2 |
| 0·01031 | 2·2895 | 0·87699 | 1·65 | 0·356 | 1·49834 | 0·33443 | 48·8 |
| 0·01240 | 2·2934 | 0·87771 | 1·68 | 0·363 | 1·49850 | 0·33424 | 47·8 |
| | | | *o-Bromobenzenediazocyanide.* | | | | |
| | | | Labile form (*cis*-). | | | | |
| 0·01417 | 2·3814 | 0·87997 | 7·69 | 0·500 | 1·49864 | 0·33346 | 47·0 |
| 0·02509 | 2·4710 | 0·88447 | 7·91 | 0·488 | 1·49956 | 0·33229 | 47·5 |
| | | | Stable form (*trans*-). | | | | |
| 0·00665 | 2·3730 | 0·87642 | 15·11 | 0·454 | 1·49803 | 0·33447 | 52·7 |
| 0·01186 | 2·4532 | 0·87853 | 15·23 | 0·458 | 1·49846 | 0·33391 | 50·6 |
| | | | 2 : 4 : 6-*Tribromobenzenediazocyanide.* | | | | |
| | | | Labile form (*cis*.-) | | | | |
| 0·00642 | 2·2861 | 0·87726 | 2·12 | 0·620 | 1·49781 | 0·33402 | 65·5 |
| 0·00874 | 2·2904 | 0·87852 | 2·05 | 0·620 | 1·49790 | 0·33359 | 62·5 |
| | | | Stable form (*trans*-). | | | | |
| 0·00729 | 2·3085 | 0·87769 | 4·94 | 0·614 | 1·49793 | 0·33393 | 67·7 |

TABLE II.

| Diazobenzenecyanide derivative. | M. p. | $M$. | $\alpha\epsilon_2$. | $\beta$. | $P_\infty$. | $[R_L]_D$. | $\mu$. |
|---|---|---|---|---|---|---|---|
| *cis-p*-Chloro- | 29° | 165·5 | 5·97 | 0·325 | 224 | 46·1 | 2·93 |
| *trans-p*-Chloro- | 105 | 165·5 | 9·52 | 0·322 | 335 | 48·0 | 3·73 |
| *cis-p*-Bromo- | 42—43 | 210 | 4·71 | 0·457 | 225 | 49·9 | 2·91 |
| *trans-p*-Bromo- | 132 | 210 | 7·80 | 0·444 | 348 | 52·3 | 3·78 |
| *cis-p*-Nitro- | 29—30 | 176 | 2·92 | 0·369 | 134 | 44·7 | 2·04 |
| *trans-p*-Nitro- | 86 | 176 | 1·67 | 0·359 | 94 | 48·6 | 1·47 |
| *cis-o*-Bromo- | 52—53 | 210 | 7·80 | 0·494 | 344 | 47·2 | 3·79 |
| *trans-o*-Bromo- | 109 | 210 | 15·17 | 0·456 | 638 | 51·6 | 5·32 |
| *cis*-2 : 4 : 6-Tribromo- | 59—60 | 368 | 2·09 | 0·620 | 192 | 64 | 2·5 |
| *trans*-2 : 4 : 6-Tribromo- | 149 | 368 | 4·94 | 0·614 | 390 | 68 | 4·0 |

in acetic acid (Hantzsch, *Ber.*, 1901, **34**, 3339) and precipitation with ether. It was dissolved in aqueous alcohol and treated with an equimolecular quantity of potassium cyanide solution. (Hantzsch and Danziger, *loc. cit.*; Ciusa, *loc. cit.*) The pale yellow *cis*-diazocyanide was formed slowly, but it was filtered off and washed as soon as possible on account of the tendency of a diazocyanide to combine with hydrogen cyanide, with the formation of a diazoimidocyanide (Gabriel, *Ber.*, 1879, **12**, 1637; Hantzsch and Schultze, *loc. cit.*). Recrystallisation in the previous manner from light petroleum gave small, pale yellow plates of the *cis*-diazocyanide, which was found to isomerise spontaneously at 57·5° in benzene solution, then becoming intensely red.

The m. p.'s of the various materials, included in Table II, were in substantial agreement with those recorded by Hantzsch and his collaborators, but were slightly higher in some cases.

The absorption spectra of the isomeric *p*-bromobenzenediazocyanides in benzene solution, shown in Fig. 4, were obtained with a Hilger quartz spectrograph E.2 and a Spekker photometer.

FIG. 4.

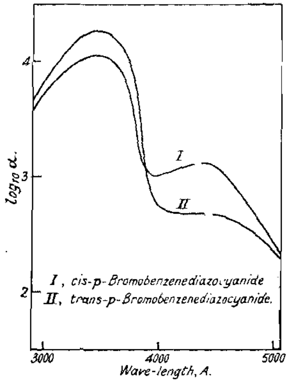
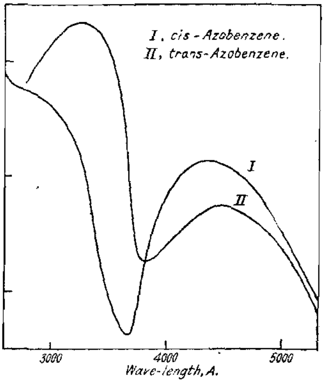



FIG. 5.




They are very similar in form, but differ in the intensity of the absorption bands. The extinction coefficient, $\alpha$, is defined by $\log_{10} I_0/I = \alpha cl$, where $c$ is the concentration in g.-mols./l. and $l$ is in cm. The spectra of the two forms of azobenzene (Fig. 5), specimens of which were kindly provided by Dr. G. S. Hartley, were obtained in the same way. In *cis*-azobenzene the ultraviolet absorption band is considerably shifted towards a higher frequency, but an analogous effect has been observed in other cases of geometrical isomerism; the isomeric diazotates provide an example (Dobbie and Tinkler, J., 1905, **87**, 276; Hantzsch and Lifschitz, *loc. cit.*; Cambi and Szegö, *Ber.*, 1928, **61**, 2081).

*Dielectric-polarisation Measurements.*—The required observations are recorded in Table I under the usual headings: $w_1$ the weight fraction, $d_{4^\circ}^{25^\circ}$ the density, $\epsilon_{1300}^{25^\circ}$ the dielectric constant, $n_D^{25^\circ}$ the refractive index, and $r_{12}$ the specific refraction. The results have been calculated from the equation (Le Fèvre and Vine, J., 1937, 1809) $P_\infty = Mp_\infty = M[p_2(1-\beta) + C\alpha\epsilon_2]$, the mean values of $\alpha\epsilon_2$ and $\beta$ involved being tabulated in cols. 4 and 5 of Table II.

The following constants were employed: $p_2 = 0{\cdot}3409$, $C = 0{\cdot}1881$.

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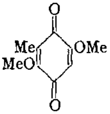
## 86. *The Isomeric Dimethoxy-2 : 5-toluquinones and Certain Related Compounds.*

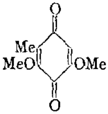
By W. K. Anslow, J. N. Ashley, and H. Raistrick.

Methods are given for the synthesis of the three isomeric dimethoxy-2 : 5-toluquinones, *i.e.*, 3 : 6-*dimethoxytoluquinone*, 4 : 6-*dimethoxytoluquinone*, and 3 : 4-*dimethoxytoluquinone*, and also for 4-*hydroxy-6-methoxytoluquinone* and 6-hydroxy-4-methoxytoluquinone and their corresponding quinols.

Fumigatin, a hitherto undescribed mould metabolic product, has recently been isolated in these laboratories from cultures of the mould *Aspergillus fumigatus* Fresenius (Anslow and Raistrick, *Biochem. J.*, 1938, **32**, 687). It has the empirical formula $C_8H_8O_4$, and has been shown by analytical methods to be a monohydroxymonomethoxy-2 : 5-toluquinone. During the course of the investigation of its molecular constitution it became necessary to synthesise each of the three isomeric *dimethoxy*-2 : 5-*toluquinones* (I, II, and III), since none of these had been described previously.




(I.)

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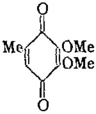


(III.)

(I) melts at 104—105°, (II) at 125°, and (III) at 59°. Fumigatin methyl ether, m. p. 59°, must have structure (III), since its melting point is not depressed by (III). (I) and (II) are orange-yellow to golden in colour, and (III) is bright red.

(I) was prepared by the methylation of 3 : 6-dihydroxytoluquinone (Fichter and Glaser, *Annalen*, 1908, **361**, 400). The method of preparation of Fichter's quinone—treatment of toluquinone with methylamine and hydrolysis of the resulting bismethylaminotoluquinone with sulphuric acid—leaves its orientation somewhat uncertain, but since the orientation of (II) and (III) is indisputable, the orientation of (I) follows and hence also, that of Fichter's dihydroxytoluquinone.

(II) was prepared from 6-methoxytoluquinone (Majima and Okazaki, *Ber.*, 1916, **49**, 1490) and from 4-methoxytoluquinone (Luff, Perkin, and Robinson, J., 1910, **97**, 1137; Ashley, J., 1937, 1471). In each case a hydroxy-group was introduced into the molecule by means of the Thiele–Winter reaction (*Annalen*, 1900, **311**, 341) and hydrolysis of the resulting triacetate. The phenol so formed was oxidised to the corresponding quinone with ferric chloride, and the above-introduced hydroxy-group was methylated with methyl sulphate. Since the resulting dimethoxytoluquinone was the same in each case, it follows that the two methoxy-groups in this quinone must be in the *o*- and *p*-positions to the methyl group, *i.e.*, that the dimethoxytoluquinone must have structure (II).

(III) was prepared by the reduction of 5-nitrohomoveratrole (5-nitro-3 : 4-dimethoxytoluene) (Oberlin, *Arch. Pharm.*, 1925, **263**, 662) to 5-aminohomoveratrole and oxidation of the amino-compound with sodium dichromate and sulphuric acid.

### Experimental.

3 : 6-*Dimethoxy*-2 : 5-*toluquinone* (I).—3 : 6-Dihydroxytoluquinone (Fichter and Glaser, *loc. cit.*) (0·4 g.) was heated for 3 hours with a mixture of anhydrous potassium carbonate (1·5 g.), methyl sulphate (1 ml.), and acetone (20 ml.). A further 1·5 g. of potassium carbonate and 1 ml. of methyl sulphate were then added, and the heating continued for a further 4½ hours. The mixture was cooled, filtered, the solvent removed, and the product extracted with boiling light petroleum (b. p. 40—50°). It was purified by sublimation in a high vacuum, followed by crystallisation from light petroleum (b.p. 40—50°), containing a little methanol, and was finally obtained by vacuum sublimation as orange-yellow clusters of needles, m. p. 104—105°. The

yield was small (Found: C, 59·1; H, 5·3; O·CH$_3$, 32·4. $C_9H_{10}O_4$ requires C, 59·3; H, 5·5; 2O·CH$_3$, 34·1%). It gives a purple colour with concentrated sulphuric acid and a reddish-purple with 2N-sodium hydroxide.

4 : 6-*Dimethoxy*-2 : 5-*toluquinone* (II).—(a) *From* 6-*methoxytoluquinone*. 3-Nitro-2-hydroxytoluene, prepared from *o*-cresol by nitration in glacial acetic acid, was methylated by heating with a mixture of methyl sulphate, potassium carbonate, and toluene. The resulting 3-nitro-2-methoxytoluene was reduced to 3-amino-2-methoxytoluene with tin and hydrochloric acid (Hofmann and v. Miller, *Ber.*, 1881, **14**, 570). 3-Amino-2-methoxytoluene (14 g.) was dissolved in a cold mixture of concentrated sulphuric acid (98 ml.) and water (280 ml.) and to it was added a suspension of potassium dichromate (14 g.) in water (80 ml.). The mixture was kept cold and well stirred. On the following day a further quantity of potassium dichromate (28 g.) in water (160 ml.) was added under the same conditions. After 4 hours the mixture was extracted with ether, the extract dried over magnesium sulphate, and the ether removed. The dark residue was distilled in a vacuum to give a yellow oil (b. p. about 130°/15 mm.), which solidified later, m. p. 19—20°. Yield from 34 g. of crude amine, 5·5 g. This quinone is the same as that prepared by Majima and Okazaki (*Ber.*, 1916, **49**, 1490), but the Japanese workers did not record any m. p.

The above quinone (5·5 g.) was dissolved in a mixture of acetic anhydride (55 ml.) and concentrated sulphuric acid (2·5 ml.). After 2—3 days it was poured into ice and water; the oil obtained quickly solidified (7·6 g.). 3 : 4 : 6-*Triacetoxy*-2-*methoxytoluene* crystallised from methanol in clusters of colourless plates, m. p. 98—99° (Found: C, 56·8; H, 5·5; O·CH$_3$, 10·3. $C_{14}H_{16}O_7$ requires C, 56·7; H, 5·5; O·CH$_3$, 10·5%).

The triacetate (6 g.) was refluxed for ½ hour with methanol (30 ml.) and concentrated sulphuric acid (1 ml.) in an atmosphere of nitrogen. Water was added, and the methanol removed by distillation in a vacuum. The 3 : 4 : 6-*trihydroxy*-2-*methoxytoluene* was extracted with ether, and purified by sublimation in a high vacuum. Yield of crude phenol, 3·8 g. The pure phenol is a colourless product, m. p. 146—147°. It gives a lemon-yellow colour with concentrated sulphuric acid and an apple-green colour with 2N-sodium hydroxide, which changes first to brown and then to cherry-red on standing (Found: C, 56·5; H, 5·9; O·CH$_3$, 17·8. $C_8H_{10}O_4$ requires C, 56·5; H, 5·9; O·CH$_3$, 18·2%).

The above crude phenol (2 g.) was dissolved in water (3 ml.) and to this solution were added 10 ml. of a solution of ferric chloride (50 g.) in water (110 ml.). The 4-*hydroxy*-6-*methoxy*-2 : 5-*toluquinone*, which quickly separated, was filtered off immediately, washed with saturated sodium chloride solution, dried in a vacuum, and sublimed in a high vacuum to give microscopic bunches of orange needles (0·94 g.), m. p. 116° (Found: C, 57·2; H, 5·0; O·CH$_3$, 18·4. $C_8H_8O_4$ requires C, 57·1; H, 4·8; O·CH$_3$, 18·5%). It gives a pure blue colour with concentrated sulphuric acid and a deep cherry-red with 2N-sodium hydroxide [indistinguishable from that given by (II)]. A mixtnre with fumigatin (m. p. 116°) melted at 97°.

The above quinone (0·2 g.) was methylated by heating for 3 hours with acetone (5 ml.), methyl sulphate (1 ml.), and anhydrous potassium carbonate (1 g.). The mixture was dilnted with ether (50 ml.) and filtered. On evaporation the crude 4 : 6-*dimethoxy*-2 : 5-*toluquinone* (II) crystallised. It was extracted with light petroleum (b. p. 40—50°) and sublimed in a high vacuum to give 0·12 g. of orange-coloured material, m. p. 118°. This was recrystallised from light petroleum (b. p. 40—50°) to give golden needles with a constant m. p. of 125° (Found: C, 59·2; H, 5·6; O·CH$_3$, 34·1. $C_9H_{10}O_4$ requires C, 59·3; H, 5·5; 2O·CH$_3$, 34·1%). It gives a deep violet-blue colour with concentrated sulphuric acid and a deep cherry-red with 2N-sodium hydroxide.

(b) *From* 4-*methoxytoluquinone*. 4-Methoxytoluquinone (10 g.), prepared from toluquinone by the method of Ashley (*loc. cit.*), was suspended in a mixture of acetic anhydride (100 ml.) and concentrated sulphuric acid (5 ml.) and kept at room temperature for 2 days with occasional shaking. The mixture was then poured into water and worked up in the usual way. 2 : 3 : 6-Triacetoxy-4-methoxytoluene (18·5 g.) formed colourless needles, m. p. 89—90°, from 50% aqueous acetic acid (Erdtman, *Proc. Roy. Soc.*, 1933, *A*, **143**, 188, gives 91—92°). This triacetate was described by Erdtman as 2 : 3 : 5-triacetoxy-4-methoxytoluene, but in a private communication to us of work which he has not yet published he agrees that it is 2 : 3 : 6-triacetoxy-4-methoxytoluene.

The triacetate (6 g.) was refluxed for ½ hour in an atmosphere of nitrogen with a mixture of methanol (30 ml.) and concentrated sulphuric acid (1 ml.). Water was added, and the methanol removed by distillation in a vacuum. The 2 : 3 : 6-trihydroxy-4-methoxytoluene was extracted with ether and purified by sublimation in a high vacuum (yield of crude phenol, almost

*theoretical*). The pure *phenol* is a pale cream solid, m. p. 150° (some decomp.). It gives a lemon-yellow colour with concentrated sulphuric acid. With 2N-sodium hydroxide it gives at first a green colour, which quickly becomes brownish-green, then brownish-purple, and finally violet (Found: C, 56·6; H, 5·9; O·$CH_3$, 18·4. Calc. for $C_8H_{10}O_4$: C, 56·5; H, 5·9; O·$CH_3$, 18·2%).

The crude phenol (0·5 g.), dissolved in water (20 ml.), was treated with 2·5 ml. of a solution of ferric chloride (50 g.) in water (110 ml.). 6-Hydroxy-4-methoxytoluquinone separated as a golden-brown solid (yield, almost theoretical), which was sublimed in a high vacuum, forming brownish-orange prisms, m. p. 203—204° (decomp. with partial sublimation). It gives an intense violet colour with 2N-sodium hydroxide and an intense violet-blue colour with concentrated sulphuric acid (Found: C, 57·3; H, 4·9; O·$CH_3$, 18·4. Calc. for $C_8H_8O_4$: C, 57·1; H, 4·8; O·$CH_3$, 18·5%). 6-Hydroxy-4-methoxytoluquinone has been prepared previously by Konya (*Monatsh.*, 1900, **21**, 422) by oxidising 3-amino-2 : 6-dihydroxy-4-methoxytoluene with ferric chloride and by Pollak and Solomonica (*Monatsh.*, 1901, **22**, 1008) by oxidising 3-amino-2-hydroxy-4 : 6-dimethoxytoluene with ferric chloride. Konya records the m. p. as 186° and Pollak and Solomonica as 183—185°. We have repeated Konya's work, starting as he did with methyl phloroglucinol, and have succeeded in raising the m. p. to 204° by subliming the resulting 6-hydroxy-4-methoxytoluquinone in a high vacuum. This m. p. was not depressed by 6-hydroxy-4-methoxytoluquinone prepared from 4-methoxytoluquinone as described above. Further, the quinol 2 : 3 : 6-trihydroxy-4-methoxytoluene, prepared by the reduction of either of our specimens of 6-hydroxy-4-methoxytoluquinone and sublimed in a high vacuum, melted at 150°, either alone or as a mixture. Konya gives the m. p. as 134°.

4 : *6-Dimethoxytoluquinone*.—6-Hydroxy-4-methoxytoluquinone (0·5 g.) was methylated by heating for 3 hours with a mixture of acetone (12·5 ml.), methyl sulphate (2·5 ml.), and anhydrous potassium carbonate (2·5 g.). The reaction mixture was diluted with ether (50 ml.) and filtered. The ether was removed, leaving an oil, which was extracted with boiling light petroleum (300 ml., b. p. 40—50°). On cooling, long golden needles (0·15 g.) were deposited, m. p. 123°. A portion was sublimed in golden needles, m. p. 125°. This m. p. was not depressed by 4 : 6-dimethoxytoluquinone (m. p. 125°) prepared from 4-hydroxy-6-methoxytoluquinone.

*6-Acetoxy-4-methoxytoluquinone*.—6-Hydroxy-4-methoxytoluquinone does not undergo the usual Thiele–Winter reaction. Instead, the hydroxy-group is acetylated and *6-acetoxy-4-methoxytoluquinone* is formed. 6-Hydroxy-4-methoxytoluquinone (0·1 g.) was dissolved in 1·5 ml. of a mixture of acetic anhydride (30 ml.) and concentrated sulphuric acid (1 ml.), kept for 3 days, and poured into ice-water. There was an immediate separation of lemon-yellow needles (0·09 g.), which were purified by sublimation in a high vacuum, giving lemon-yellow prisms, m. p. 139° (Found: C, 57·3; H, 4·9; O·$CH_3$, 14·9. $C_{10}H_{10}O_5$ requires C, 57·1; H, 4·8; O·$CH_3$, 14·8%).

3 : *4-Dimethoxy-2 : 5-toluquinone* (*Fumigatin Methyl Ether*) (III).—Vanillin was reduced to creosol, which was nitrated to give 5-nitrocreosol by the method of Oberlin (*Arch. Pharm.*, 1925, **263**, 662). A mixture of 5-nitrocreosol (23 g.), potassium carbonate (45 g.), methyl sulphate (22 ml.), and toluene (160 ml.) was refluxed for 3 hours. A further 22 ml. of methyl sulphate were added during the next 1½ hours and the heating was continued for a total period of 6 hours. The reaction mixture was diluted with toluene, washed with 2% sodium hydroxide solution, and dried. The toluene was removed, and the residue purified by distillation in a vacuum to give 22 g. of 5-nitrohomoveratrole.

5-Nitrohomoveratrole (12·5 g.) was reduced to 5-aminohomoveratrole by refluxing for 1 hour with a mixture of concentrated hydrochloric acid (37·5 ml.), water (12·5 ml.), ethanol (25 ml.), and granulated tin (17·5 g.). The alcohol was removed in a vacuum, a solution of sodium hydroxide (31 g.) in water (125 ml.) added, and the whole extracted with ether. On removal of the ether, a pale brown oil (8 g.) remained and this was converted into the quinone without further purification. It was dissolved in a cold mixture of concentrated sulphuric acid (32 ml.) and water (100 ml.), placed in a freezing mixture, and a solution of sodium dichromate (5 g.) in water (30 ml.) was slowly added with constant stirring. The following day a further 10 g. of sodium dichromate in 60 ml. of water were added under the same conditions. After 3 hours, the mixture was extracted with ether. On removal of the solvent a reddish-black oil (2·6 g.) remained and quickly crystallised. It was sublimed in a high vacuum (bath temperature 46—48°), 3 : *4-dimethoxytoluquinone* being obtained in beautiful red needles, m. p. 59°, alone or mixed with fumigatin methyl ether (Found: C, 59·4; H, 5·6; O·$CH_3$, 34·0. $C_9H_{10}O_4$ requires C, 59·3; H, 5·5; 2O·$CH_3$, 34·1%). With concentrated sulphuric acid it gives at once a dark brown colour, changing to cherry-red in a few minutes, and becoming an intense purple on

standing. The same sequence of colour changes is given by fumigatin. With 2N-sodium hydroxide it gives a brown colour which slowly fades on standing.

We desire to thank Dr. G. Rotter of the Research Department, Woolwich, and also the I.G. Farbenindustrie A.G., for gifts of methyl phloroglucinol, and Dr. A. R. Chambers for assistance in the preparation of 6-hydroxy-4-methoxytoluquinone from methyl phloroglucinol. We also gratefully acknowledge much friendly correspondence with, and many suggestions from, Dr. H. Erdtman, College of Technology, Stockholm.

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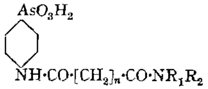
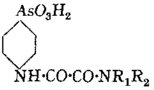
## 87. *New Derivatives of* p-*Arsanilic Acid. Part VIII.* p-*Arsono-oxanilic and* p-*Arsonohexadecanedicarboxylanilic Acids and Related Compounds.*

By Sir GILBERT MORGAN and ERIC WALTON.

Compounds of type (1) have shown considerable trypanocidal activity throughout the series from $n = 1$ to 8. The activity was at its maximum where $n = 1$, 2, and 3, and tended to diminish higher in the series. This research has now been concluded by the preparation of an oxalyl series ($n = 0$), and one or two compounds where $n = 16$.

THE group of compounds of type (I), described from time to time in this Journal, has now been completed, for all practical purposes, at one end of the series by the synthesis of several

(I.) 

 (II.)

compounds (11) containing an oxalyl residue, and at the other end by the preparation of one or two compounds where $n = 16$ (1).

The oxalyl compounds were readily obtained by treating the *methyl* ester of *p*-arsono-oxanilic acid (Bertheim, *Ber.*, 1911, **44**, 3092) with various amines, but compounds in the hexadecanedicarboxylyl series were much more difficult to prepare. p-*Arsonohexadecanedicarboxylanilic acid*, $AsO_3H_2{\cdot}C_6H_4{\cdot}NH{\cdot}CO{\cdot}[CH_2]_{16}{\cdot}CO_2H$, was obtained in small yield by Schotten–Baumann methods, but, owing to hydrolysis, only traces of its *methyl* ester could be prepared directly by similar methods. Crude methyl ester was eventually obtained in better yield by esterification of the arsonic acid, but neither acid nor ester could be converted into amides.

As might be expected, owing to the exceptional toxicity of oxalic acid, the oxalyl series proved rather more toxic than is usual where $n$ (in I) is low, but in regard to trypanocidal activity, they were still found more or less true to type. We are indebted to Professor Warrington Yorke, F.R.S., for the following summary of pharmacological tests on mice.

*Oxalyl Series.*

| Sodium salts. | M.L.D. | M.C.D. |
|---|---|---|
| Amide | 8 | Some action in maximum doses |
| Methylamide | 4 | Some action in maximum doses |
| Dimethylamide | 64 | 16–32 |
| Ethylamide | 16 | Some action in maximum doses |

| Sodium salts. | M.L.D. | M.C.D. |
|---|---|---|
| *n*-Propylamide | 4 | Some action in maximum doses |
| Piperidide | 20 | Some action in maximum doses |
| Anilide | 4 | Inactive |
| *p*-Arsonohexadecanedicarboxylanilic acid | 16 | Inactive |

M.L.D. = minimum lethal dose, M.C.D. = minimum curative dose, both in mg. per 20 g. of mouse.

## Experimental.

### *Oxalyl Derivatives.*

*Methyl* p-*Arsono-oxanilate.*—*p*-Arsono-oxanilic acid (Bertheim, *loc. cit.*) (83 g.), methyl alcohol (240 c.c.), and sulphuric acid (2·5 c.c.) were refluxed together for 5 hours. The *methyl* p-*arsono-oxanilate* was collected and washed with dilute hydrochloric acid to remove *p*-arsanilic acid. It crystallised from water in glistening rhombic plates (47 g.), only slightly soluble in alcohol (Found: As, 25·5; O·CH$_3$, 9·7. $C_9H_{10}O_6NAs$ requires As, 24·8; O·CH$_3$, 10·2%). The sodium salt could not be obtained, as the methyl ester was found to be unstable in neutral and in alkaline solutions.

*Ethyl* p-*Arsono-oxanilate.*—Carbethoxyformyl chloride (18 g.), *p*-arsanilic acid (32 g.) in a little water, and 2N-sodium hydroxide (150 c.c.) were shaken together, acidified, and the solid collected and crystallised from water plus a trace of hydrochloric acid (yield, 15 g.). *Ethyl* p-*arsono-oxanilate* is dimorphous. It crystallised from rapidly cooled water in long needles, which, at room temperature, slowly changed to octagonal platelets, slightly soluble in alcohol (Found: As, 24·1. $C_{10}H_{12}O_6NAs$ requires As, 23·7%). The sodium salt was gelatinous, but too unstable for analysis.

*Oxanilamide*-p-*arsonic Acid* (Jacobs and Heidelberger, *J. Amer. Chem. Soc.*, 1919, **41**, 1597).—Methyl *p*-arsono-oxanilate (2 g.) was stirred into excess of concentrated aqueous ammonia. The latter was removed, and the residue acidified. The amide, thus obtained, crystallised from water in slender prisms, insoluble in alcohol (Found: hydrolysable N, 4·95. Calc. for $C_8H_9O_5N_2As$: hydrolysable N, 4·9%). The *sodium* salt crystallised from dilute alcohol in large prisms (Found: hydrolysable N, 4·7. $C_8H_8O_5N_2AsNa$ requires hydrolysable N, 4·5%).

*Oxanilomethylamide*-p-*arsonic Acid.*—The methyl ester (3 g.) and an excess of 33% aqueous methylamine were warmed together for 1 minute. The methylamide, obtained by acidification, was purified through its *sodium* salt, $p_H$ 6·5, which crystallised from water in long silky needles (2·1 g.) (Found: hydrolysable N, 3·9. $C_9H_{10}O_5N_2AsNa,2H_2O$ requires hydrolysable N, 3·9%). *Oxanilomethylamide*-p-*arsonic acid* crystallised from water, in which it was only sparingly soluble, in minute leaflets, insoluble in alcohol (Found: hydrolysable N, 4·7. $C_9H_{11}O_5N_2As$ requires hydrolysable N, 4·6%).

*Oxanilodimethylamide*-p-*arsonic acid*, prepared by warming the methyl ester with 33% aqueous dimethylamine, crystallised from water in rhombic leaflets, insoluble in alcohol (Found: hydrolysable N, 4·45. $C_{10}H_{13}O_5N_2As$ requires hydrolysable N, 4·4%). The *sodium* salt crystallised from dilute alcohol in fine needles, $p_H$ 6·5 (Fonnd: hydrolysable N, 3·85. $C_{10}H_{12}O_5N_2AsNa,H_2O$ requires hydrolysable N, 3·9%).

*Oxaniloethylamide*-p-*arsonic acid*, prepared as above from 33% aqueous ethylamine, crystallised from water in flocculent micro-needles, insoluble in alcohol (Found: hydrolysable N, 4·3. $C_{10}H_{13}O_5N_2As$ requires hydrolysable N, 4·4%). The *sodium* salt crystallised from dilute alcohol in hexagonal leaflets, $p_H$ 6·5 (Found: hydrolysable N, 3·9. $C_{10}H_{12}O_5N_2AsNa,H_2O$ requires hydrolysable N, 3·9%).

*Oxanilo*-n-*propylamide*-p-*arsonic Acid.*—Methyl *p*-arsono-oxanilate (8 g.) and an excess of 30% aqueous *n*-propylamine were heated at 100° in a sealed tube for 2 honrs. The solution was evaporated and acidified, and the resulting n-*propylamide* collected and crystallised from water, forming rectangular plates, slightly soluble in alcohol (Found: hydrolysable N, 4·2. $C_{11}H_{15}O_5N_2As$ requires hydrolysable N, 4·2%). The *sodium* salt crystallised from 50% aqueons alcohol in minute needles, $p_H$ 7·5 (Found: hydrolysable N, 4·0. $C_{11}H_{14}O_5N_2AsNa$ requires hydrolysable N, 4·0%).

*Oxanilopiperidide*-p-*arsonic Acid.*—The methyl ester (2 g.) and an excess of 50% aqueous piperidine, warmed and acidified, yielded the *piperidide*, which crystallised from water in feathery needles (1·2 g.), soluble in alcohol (Found: hydrolysable N, 3·7. $C_{13}H_{17}O_5N_2As$ requires hydrolysable N, 3·9%). The *sodium* salt crystallised from dilute alcohol in long silky needles, $p_H$ 6·5 (Found: hydrolysable N, 3·5. $C_{13}H_{16}O_5N_2AsNa,H_2O$ requires hydrolysable N, 3·5%).

*Oxanilide*-p-*arsonic Acid.*—The methyl ester (5 g.) and an excess of aniline (20 c.c.) were boiled together until a cream-coloured solid separated from the clear solution. The mixture was acidified, and the solid collected and washed with water and alcohol (yield, 4·5 g.). The crude anilide was converted into its *disodium* salt, which crystallised from alcohol–water in long silky needles, $p_H$ 9·0 (Found: As, 17·6. $C_{14}H_{11}O_5N_2AsNa_2,H_2O$ requires As, 17·6%). The pure *anilide*, from its sodium salt, was a gelatinous solid, which, although almost insoluble, was readily changed into micro-needles on boiling with water. It was insoluble in alcohol (Found: As, 20·8, 20·75. $C_{14}H_{13}O_5N_2As$ requires As, 20·6%).

*Aniline Salts of* p-*Arsono-oxanilic Acid.*—Three well-defined *salts* were formed on boiling together, in water, *p*-arsono-oxanilic acid and various proportions of aniline. (1) With a trace of aniline, long silky needles, corresponding with the formula $2AsO_3H_2\cdot C_6H_4\cdot NH\cdot CO\cdot CO_2H,C_6H_5\cdot NH_2$ were formed (Found: As, 22·5. $C_{22}H_{23}O_{12}N_3As_2$ requires As, 22·4%). (2) With more aniline, glistening rhombs having the formula $AsO_3H_2\cdot C_6H_4\cdot NH\cdot CO\cdot CO_2H,C_6H_5\cdot NH_2$ were obtained (Found: As, 20·2. $C_{14}H_{15}O_6N_2As$ requires As, 19·6%). (3) With excess of aniline, $AsO_3H_2\cdot C_6H_4\cdot NH\cdot CO\cdot CO_2H,2C_6H_5\cdot NH_2$ was formed in long prisms (Found: As, 16·1. $C_{20}H_{22}O_6N_3As$ requires As, 15·8%).

### *Hexadecanedicarboxylyl Derivatives.*

Methyl hexadecane-αω-dicarboxylate (Chuit, *Helv. Chim. Acta*, 1926, **9**, 264) was prepared by electrolysis of equimolecular proportions of methyl hydrogen sebacate and potassium hydroxide (5N) in small batches (about 20 c.c.) according to the method of Brown and Walker (*Annalen*, 1891, **261**, 125). The material was, however, electrolysed in boiling tubes instead of a platinum crucible, a platinum plate forming the anode. The oily layer, after extraction with ether and three recrystallisations from light petroleum (b. p. 60—80°), gave methyl hexadecanedicarboxylate in leaflets, m. p. 53—56° (yield, 10 g. from 240 g. of methyl hydrogen sebacate) (Found: $O\cdot CH_3$, 16·65. Calc. for $C_{20}H_{38}O_4$: $O\cdot CH_3$, 18·1%).

*Methyl Hydrogen Hexadecane-αω-dicarboxylate.*—The methyl ester (13·6 g.) in methyl alcohol was treated carefully with 2·25 g. of potassium hydroxide in methyl alcohol. The mixture was evaporated to dryness, and the residue dissolved in water and acidified. The precipitate was crystallised from light petroleum (b. p. 60—80°), whereby three fractions were obtained: (1) an insoluble residue, m. p. 122—124°, consisting largely of dicarboxylic acid, (2) a fraction, crystallising on cooling and consisting largely of *methyl hydrogen hexadecanedicarboxylate*, and (3) mother-liquor, containing mainly methyl ester. Recrystallisation of (2) gave minute needles of the methyl hydrogen ester (6 g.), m. p. 72—74° (Found: C, 69·4; H, 11·0; $O\cdot CH_3$, 7·9. $C_{19}H_{36}O_4$ requires C, 69·5; H, 11·0; $O\cdot CH_3$, 9·4%).

p-*Arsonohexadecanedicarboxylanilic Acid.*—Hexadecanedicarboxylic acid (9 g.) was treated with excess of thionyl chloride for 24 hours. After removal of the thionyl chloride, the residue was vigorously shaken with sodium *p*-arsanilate (10 g.) in water (100 c.c.), sodium carbonate being added from time to time to maintain alkalinity. The solid, obtained by acidification, was dried, extracted with chloroform until the weight was constant, and finally ground with dilute hydrochloric acid (yield, 7 g.). The *acid* was further purified through alcohol (in which it is soluble), and was indefinitely crystalline. On treatment with thionyl chloride, it decomposed at the ·NH·CO· linkage (Found: As, 13·7. $C_{24}H_{40}O_6NAs$ requires As, 14·6%).

The insoluble residue from the alcohol treatment was brown and gelatinous, but its analysis corresponded roughly with *hexadecanedicarboxylanilide*-pp′-*diarsonic acid*,

$$AsO_3H_2\cdot C_6H_4\cdot NH\cdot CO\cdot [CH_2]_{16}\cdot CO\cdot NH\cdot C_6H_4\cdot AsO_3H_2$$

(Found: As, 19·4. $C_{30}H_{46}O_8N_2As_2$ requires As, 21·1%). *Sodium* p-*arsonohexadecanedicarboxylanilate* separated from dilute alcohol as an amorphous solid, giving soapy solutions in warm water. In cold water, it apparently formed a colloidal suspension, $p_H$ 7·5 (Found: As, 12·85. $C_{24}H_{38}O_6NAsNa_2$ requires As, 13·4%).

*Methyl* p-*Arsonohexadecanedicarboxylanilate.*—Methyl hydrogen hexadecanedicarboxylate (6·5 g.), treated with thionyl chloride (3 c.c.) for 24 hours, yielded its *acid chloride*, which crystallised from light petroleum (b. p. 60—80°) in tufts of micro-needles (Found: Cl, 9·6. $C_{19}H_{35}O_3Cl$ requires Cl, 10·2%). When, however, this acid chloride was shaken with sodium *p*-arsanilate and alkali in the usual way, it yielded mainly *p*-arsonohexadecanedicarboxylanilic acid and only traces of the corresponding methyl ester. Attempts to prepare *methyl* p-*arsonohexadecanedicarboxylanilate* by esterification with hydrogen chloride were also unsuccessful, owing to hydrolysis at the ·NH·CO· linkage, but the crude ester was eventually obtained by refluxing the free acid with methyl alcohol and a trace of sulphuric acid (Found: As, 13·8; $O\cdot CH_3$, 4·0. $C_{25}H_{42}O_6NAs$ requires As, 14·2; $O\cdot CH_3$, 5·9%). A soluble sodium salt of the ester could not be obtained.

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Chemical Research Laboratory, Teddington, Middlesex. [*Received, February 28th, 1938.*]

# 88. *Mechanism of Aromatic Side-chain Reactions with Special Reference to the Polar Effects of Substituents. Part IX. The* ortho-*Effect in the Reaction of Phenacyl Bromides with Pyridine.*

By John W. Baker.

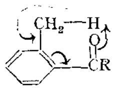
The reaction $C_6H_4R{\cdot}CO{\cdot}CH_2Br + NC_5H_5 \longrightarrow C_6H_4R{\cdot}CO{\cdot}CH_2{\cdot}\overset{+}{N}C_5H_5\}\overset{-}{Br}$ in 0·25M-solution in dry acetone is bimolecular and is facilitated by electron recession from the side chain to the aromatic nucleus (cf. Baker, J., 1933, 1128).

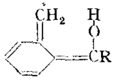
The bimolecular velocity coefficients ($k$) for phenacyl bromide and its *p*- and *o*-methyl and 2 : 4-dimethyl derivatives decrease in the order given, although the depression in the value of $k$ caused by such substitution is relatively small. The 2 : 4 : 6-trimethyl derivative (in which both ortho-positions are substituted), however, fails to undergo detectable reaction under the given experimental conditions (20°) even after five days. An explanation of these results is advanced on the basis of the occurrence of resonance between the carbonyl group and the *o*-methyl substituent (cf. Baker, J., 1935, 1844; Dippy, Evans, Gordon, Lewis, and Watson, J., 1937, 1421).

Although substitution by a nitro-group in the *p*-position in phenacyl bromide *increases* the reaction velocity about 2·5 times, similar substitution in the *o*-position *reduces* the velocity to about one-third of that of the unsubstituted parent. In this case it seems probable that a direct effect of the negative end of the nitro-group dipole on the $-CO{\cdot}CH_2Br$ side chain is involved, since any chelation is unlikely.

In a recent paper Dippy, Evans, Gordon, Lewis, and Watson (J., 1937, 1421) suggested that an alkyl group might form a hydrogen bond with an electron-donating group such as carbonyl in the *o*-position, and cited as one example the fact that *o*-toluic acid is appreciably stronger than either its *m*- or its *p*-isomeride or than benzoic acid itself.

The postulate that resonance occurs between structures of the types (I) and (II) is, of course, a direct corollary to the mechanism of the mesomeric effect of alkyl groups suggested by Baker and Nathan (J., 1935, 1844). The presence of the essential conjugated system is clearly indicated in (I). The existence of such chelation, arising from resonance phenomena,

(I.) 

 (II.)

had been postulated by the author to explain some earlier results obtained in kinetic investigations of the reaction between various alkylphenacyl bromides and pyridine, data which it now seems desirable to put on record.

It was shown (Baker, J., 1933, 1128) that, in 90% alcohol as a solvent, the reaction $C_6H_4R{\cdot}CO{\cdot}CH_2Br + NC_5H_5 \longrightarrow C_6H_4R{\cdot}CO{\cdot}CH_2{\cdot}\overset{+}{N}C_5H_5\}\overset{-}{Br}$ is almost certainly bimolecular, and that it is facilitated by substituents (*e.g.*, *p*-nitro-) which increase electron recession from the side chain to the aromatic nucleus. These conclusions have now been confirmed in dry acetone as a solvent. The following table gives the values of the bimolecular velocity coefficients for the reaction between various substituted phenacyl bromides and pyridine, both 0·025M, in that solvent.

*Reaction between* $C_6H_4R{\cdot}CO{\cdot}CH_2Br$ *and* $C_5H_5N$ *in 0·025M-solution in dry acetone*

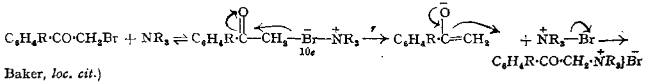
| R. | $10^3 \times k$ (l./g.-mol.-sec.). 20°. | 40°. | *E* (Arrhenius), kg.-cals. | R. | $10^3 \times k$ (l./g.-mol.-sec.). 20°. | 40°. | *E* (Arrhenius), kg.-cals. |
|---|---|---|---|---|---|---|---|
| H | 0·79 | 2·83 | 11·7 | 2 : 4 : 6-$Me_3$ | (Too slow to be measured.) | | — |
| *p*-Me | 0·74 | 2·62 | 11·6 | | | | |
| *o*-Me | 0·55 | — | — | *p*-Bu$^{\gamma}$ | 0·57 | 2·00 | 11·5 |
| 2 : 4-$Me_2$ | 0·50 | 1·82 | 11·8 | *p*-$NO_2$ | *ca.* 1·9 | — | — |
| | | | | *o*-$NO_2$ | „ 0·24 | — | — |

The anomalous effect of *o*-methyl substituents is immediately apparent. Substitution by a methyl group in one *o*-position causes a greater decrease in reaction velocity than does similar substitution in the *p*-position; but whereas the effect of simultaneous *op*-substitution, in the 2 : 4-dimethyl derivative, is approximately that anticipated on an additive basis, the introduction of methyl substituents into both *o*-positions so greatly reduces the reaction velocity that, under the standard conditions used, the 2 : 4 : 6-trimethyl derivative exhibits no appreciable reaction even after 5 days.* Since the centre of reaction is the terminal side-chain bromomethyl group, it seems improbable that a purely spatial inhibition is under observation, and the enormous difference in velocity between the 2 : 4-dimethyl and the 2 : 4 : 6-trimethyl compound seems too great to be explained purely on the basis of the simple inductive effect of an additional methyl group. The intimate mechanism of the formation of the quaternary salt is unknown, but the most feasible explanation of these results is derived from the assumption that the carbonyl group, with its intrinsic capacity for polarisation in the sense C=O, is essentially involved. This view receives confirmation from the observation (Thomson and Stevens, J., 1932, 70) that phenylbromomethylsulphone (in which the sulphone group should activate the adjacent $\cdot CH_2Br$ group towards a nucleophilic reagent, but in which electromeric polarisation is excluded) does not react with either benzyldimethylamine or piperidine. In the *p*-methylphenacyl derivative the contribution of structures of the type $\overset{+}{H}CH_2{:}C_6H_4{:}C\bar{O}\cdot CH_2Br$ to the mesomeric wave-function is probably very small, a conclusion which is confirmed by the greater retarding effect of a *p-tert.*-butyl substituent. In compounds where one *o*-methyl group is present, however, structures of the type (II; R = $CH_2Br$) are readily formed when the side-chain carbonyl group is correctly orientated to the *o*-substituent: when both *o*-positions are substituted by methyl groups, the formation of the chelate ring is possible no matter what may be the rotational orientation of the side chain, the number of possible structures between which resonance may occur is increased and so, in this case, structures of type (II) may assume major importance. The incidence of such resonance when *o*-methyl substituents are present would greatly reduce the assumed mechanistic function of the carbonyl group † and so inhibit the reaction.

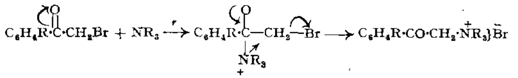
Further evidence for such interaction between the carbonyl and methyl groups is provided by the suppression of normal carbonyl activity in 2 : 4 : 6-trimethylacetophenone. Although the 2 : 4-dimethyl and the 2 : 4 : 5-trimethyl derivative readily form oximes and semicarbazones, the 2 : 4 : 6-trimethyl compound fails to react with hydroxylamine, hydrazine hydrate (Bouveault, *Compt. rend.*, 1897, **124**, 158), phenylhydrazine (Baum, *Ber.*, 1895, **28**, 3209), or semicarbazide (this communication) under the conditions ordinarily employed for the preparation of these derivatives. Neither the carbonyl group nor the bromine atom in 2 : 4 : 6-trimethylphenacyl bromide reacts with semicarbazide acetate in

* The value of *k* is of the order of $10^{-6}$—$10^{-7}$. Reaction readily occurs when the bromide is warmed with excess of pyridine without solvent.

† Examples of two *possible* mechanisms which require such polarisation of the carbonyl group and are in harmony with experimental observations are:

(1) 

(cf. Baker, *loc. cit.*)

(2) 

(cf. the mechanism of pinacolic electron displacement; Ingold and Shoppee, J., 1928, 365; Baker, "Tautomerism," p. 276 *et seq.*). In each case the assumed rate-determining stage is marked *r*. In any mechanism which involves direct attack at the carbonyl group it is obvious that purely spatial inhibitory effects may also be involved.

aqueous alcohol, but 2 : 4-dimethylphenacyl bromide readily affords a *semicarbazido*-derivative, the bromine evidently being more reactive than the carbonyl group.

Another significant example of the *ortho*-effect is provided by the relative velocities of reaction of the *o*- and *p*-nitrophenacyl bromides with pyridine. Owing to the insolubility of the quaternary salts, the values of the velocity coefficients for these two isomerides are less accurate, but there is no doubt that whereas in the *p*-position the nitro-group exerts its expected electron-attracting effect and increases the reaction velocity, yet an *o*-nitro-substituent actually reduces the velocity considerably. Although the formation of a five-membered chelate ring between an *o*-nitro-substituent and a carboxyl anion may be postulated (Dippy *et al.*, *loc. cit.*), it is difficult to assume such chelation involving a carbonyl group. Direct co-ordination of the doubly-linked oxygen (as donor) to the nitrogen as acceptor is unlikely in view of the charge distribution involved, and any other type of five-membered chelate ring necessitates tercovalent carbon.

It would thus appear that the retarding effect of an *o*-nitro-substituent must arise, in this reaction at least, from the electron-repelling effect of the negatively charged oxygen atoms of the nitro-group acting directly through the medium upon the seat of reaction in the side chain (cf. Bennett, *Chem. and Ind.*, 1935, **54**, 1008; Baker, J., 1936, 399), an effect which outweighs the electron-attractive effect (transmitted through the bonds) of the positive end of the dipole.

## EXPERIMENTAL.

*Preparation of Materials.*—*o-Methylacetophenone.* *o*-Toluoyl chloride (38 g.) was added dropwise to a solution of methylzinc iodide (0·25 g.-mol.) in benzene–ethyl acetate cooled in a freezing mixture. After being kept for 1 hour at room temperature, the reaction mixture was decomposed with ice and dilute sulphuric acid, and the ketone extracted with ether. The extract was washed with aqueous sodium carbonate and water and dried over sodium sulphate. Fractional distillation of the residue from the dried ethereal solution gave 26 g. of the ketone, b. p. 93—94°/13 mm. The semicarbazone, crystallised from alcohol, had m. p. 206° (lit., m. p. 203°; 192°). Bromination of the ketone was effected by the dropwise addition of 16 g. of bromine to 13·4 g. of the ketone, without solvent, on the steam-bath. After isolation in the usual manner, repeated fractional distillation gave the *ω-bromo*-compound, b. p. 113·5°/1·7 mm. (Found: C, 51·7, 50·4; H, 4·4, 4·3; Br, 38·5. $C_9H_9OBr$ requires C, 50·7; H, 4·2; Br, 37·6%).

2 : 4-Dimethylphenacyl bromide, m. p. 44·2—44·6°, and 2 : 4 : 6-trimethylphenacyl bromide, m. p. 57° (Found: C, 54·3; H, 5·6; Br, 33·2. Calc. for $C_{11}H_{13}OBr$: C, 54·8; H, 5·4; Br, 33·2%), were prepared by the method of Jacobs and Heidelberger (*J. Biol. Chem.*, 1915, **21**, 458). *p-tert.*-Butylacetophenone, b. p. 97—98°/0·8—0·9 mm., prepared by Verley's method (*Bull. Soc. chim.*, 1898, **19**, 73), gave a *semicarbazone*, m. p. 231—232° (decomp.) after crystallisation from 96% alcohol (Fonnd: C, 67·5; H, 8·3. $C_{13}H_{19}ON_3$ requires C, 66·9; H, 8·2%). Bromination of the ketone (8 g.) was effected by the dropwise addition of 7·9 g. of dry bromine in carbon tetrachloride solution. The solution was evaporated in a vacuum to remove most of the solvent and hydrogen bromide, and the bromide was isolated in the usual manner. Repeated fractional distillation gave p-tert.-*butylphenacyl bromide*, b. p. 127°/0·5 mm., which, however, does not seem to be pure (Found: Br, 33·2, 30·1. $C_{12}H_{15}OBr$ requires Br, 31·4%).

Bromination of *o*-nitroacetophenone in acetic acid according to Gevekoht's procedure (*Annalen*, 1883, **221**, 327) gave mainly the ωω-dibromo-derivative, m. p. 85°. The monobromo-compound was obtained by the addition of slightly less than 1 mol. of bromine to the ketone, both in solution in dry ligroin (b. p. 40—60°), gently warmed on a steam-bath. After evaporation of the solvent, the product was washed in ethereal solution with aqueous sodium bicarbonate and water, and dried with sodium sulphate. The residue from the dried ethereal solution was distilled under reduced pressure and the distillate, which crystallised, was further purified by crystallisation from cold ligroin (b. p. 40—60°) as described by Gevekoht. The sample used had m. p. 55·2°.

The samples of *p*-methyl- and *p*-nitro-phenacyl bromides were those used in an earlier investigation (Baker, J., 1932, 1148). They were again purified by crystallisation before use.

The following quaternary salts were isolated in the course of the investigation: *o-Nitrophenacylpyridinium bromide*, decomp. *ca.* 260° (Found: * Br′, 25·2. $C_{13}H_{11}O_3N_2Br$ requires Br′, 26·1%); *o-methylphenacylpyridinium bromide*, m. p. 182° (Found: * Br′, 27·1. $C_{14}H_{14}ONBr$ requires Br′, 27·4%); and 2 : 4 : 6-*trimethylphenacylpyridinium bromide*, decomp. *ca.* 280° (Found: * Br′, 24·4. $C_{16}H_{18}ONBr$ requires Br′, 25·0%), which was obtained by warming

2 : 4 : 6-trimethylphenacyl bromide with excess of pyridine without solvent, the salt which crystallised out being washed with dry acetone.

*Action of Semicarbazide Acetate.*—Under the ordinary conditions of semicarbazone formation, 2 : 4 : 6-trimethylacetophenone (von Meyer and Molz, *Ber.*, 1897, **30**, 1271) gave no semicarbazone when kept for a month. Dilution of the aqueous-alcoholic solution only reprecipitated the unchanged ketone. Addition of an alcoholic solution of the ω-bromo-compound to a solution of semicarbazide acetate gave, within a few minutes, a copious crystalline precipitate, which after crystallisation from dilute alcohol had m. p. 57° either alone or mixed with the original ω-bromo-compound. Similarly treated, 2 : 4-dimethylphenacyl bromide gave a bromine-free precipitate of the ω-*semicarbazido*-compound, m. p. 175—176°, after crystallisation from dilute alcohol (Found : N, 15·8. $C_{11}H_{15}O_2N_3,C_2H_6O$ requires N, 15·7%).

*Velocity Measurements.*—The kinetic measurements were carried out by the micro-technique previously described (Baker and Nathan, J., 1935, 1840). The values of the velocity coefficients were determined from the slope of the straight line obtained by plotting $x/(a—x)$ against time for 5—7 independent determinations of $x$. In the case of the *o*-nitro-compound, in which early crystallisation of the salt occurred, 2 c.c. samples of the reaction mixture were sealed in separate tubes kept in the thermostat, so that the whole sample could be broken into water for titration of the bromide ion formed. With 2 : 4 : 6-trimethylphenacyl bromide and pyridine, both 0·025M in dry acetone, no appreciable bromide ion could be detected in a sample taken after the reaction mixture had been kept in a thermostat at 20° for 5 days.

The bimolecular character of the reaction is confirmed by the following data obtained with various proportions of phenacyl bromide ($C_a$) and pyridine ($C_p$) :

| | | | |
|---|---|---|---|
| $C_a$, M. | 0·025 | 0·025 | 0·0125 |
| $C_p$, M. | 0·014 | 0·025 | 0·025 |
| $10^3 \times k$ | 0·78 | 0·79 | 0·79 |

All analyses, except those marked with an asterisk, are by Dr. G. Weiler.

The author thanks the Royal Society for a grant, and Dr. W. S. Nathan for carrying out some of the preliminary investigations.

The University, Leeds. [*Received, February 4th*, 1938.]

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# 89. *The Extent of Dissociation of Salts in Water. Part VII. The Conductivity of Mixtures.*

By Cecil W. Davies.

The available data for the conductivities of binary mixtures of salt solutions in water have been examined in the light of the dissociation constants derived in previous parts of this series. The large departures from additivity found with certain mixtures are always in the direction, and of the approximate magnitude, to be expected on account of mass-action effects, and therefore confirm in a semi-quantitative way the previous work on the incomplete dissociation of aqueous salt solutions. It is shown, on the other hand, that the absence of such deviations cannot be interpreted as evidence of complete dissociation.

The conductivity of mixtures of two electrolytes has been the subject of several recent studies (Smith and Gortner, *J. Physical Chem.*, 1933, **37**, 79; Van Rysselberghe and Nutting, *J. Amer. Chem. Soc.*, 1934, **56**, 1435; 1937, **59**, 333; Van Rysselberghe, Grinnell, and Carlson, *ibid.*, 1937, **59**, 336; O'Connor, *Nature*, 1937, **139**, 151), and more than one investigator has commented on effects that might be attributable to the incomplete dissociation of one or both of the electrolytes present. It seemed worth while to examine this aspect of the problem more closely, and in this paper the available data are used to test dissociation constants already derived for aqueous salt solutions, and to estimate the probable value of the method as a means of studying dissociation equilibria. Attention is confined to the type of system usually studied, in which the total electrolyte concentration is unaltered by mixing.

When two electrolyte solutions of the same equivalent concentration are mixed, the conductivity will in general differ from that calculated by the simple additive formula on account of two effects: changes in the mobilities of the ions, and, if dissociation is not complete, changes in the concentrations of the ions. The mobilities change because the rate of formation or dissipation of an ionic atmosphere is determined by the mobilities (and relative concentrations) of the ions present, so that the retardation suffered by a migrating ion on account of the "relaxation time" effect is diminished by the presence of an ion of higher mobility and increased by an ion of lower mobility. For two cations, or anions, present in approximately equal concentration, the greater absolute change will be that suffered by the ion of higher mobility, so that the net result of mixing will be a conductivity decrease which will be greater the greater the mobility difference. The quantitative theory of these mobility changes has been given by Onsager and Fuoss (*J. Physical Chem.*, 1932, **36**, 2689), but their general equation is valid only for very dilute solutions, in which the further changes attributable to incomplete dissociation effects will usually be extremely small. At higher concentrations information must be sought from the experimental data; these have been reviewed and supplemented by Van Rysselberghe and Nutting (*loc. cit.*), who quote seven mixtures of alkali-metal halides of 1-molal total concentration. In each of these mixtures dissociation can be taken as complete, and the whole conductivity change can therefore be attributed to the mobility changes. The effect at this high concentration may amount to as much as 1% of the total conductivity, but is usually less than this. In accordance with theoretical predictions, the conductivity of the mixture is always less than that given by the mixture rule, and Van Rysselberghe and Nutting find, further, that there is a rough parallelism between the maximum conductivity decrease ($\Delta\Lambda$) and the difference between the conductivities of the pure salts ($\lambda$). Though such a relation can be only very approximate, we find that the equation $\Delta\Lambda = 0{\cdot}021\lambda$ satisfies the results for these seven mixtures with an average deviation of 0·07, and a maximum deviation of 0·16 unit, and there is not much doubt that so long as the equation is not applied to mixtures containing the hydrogen ion or other ion of abnormal mobility, or to mixtures containing ions of different valency, it enables the conductivity decrease due to mobility changes to be estimated to within 0·2 unit.

Our object is now to consider mixtures in which dissociation may not be complete, and to ascertain whether the residual conductivity change, after allowance has been made for the mobility effect, is in accordance with the predictions of the incomplete dissociation theory. Van Rysselberghe and Nutting have studied five such mixtures: potassium nitrate and chloride; sodium nitrate and chloride; potassium and sodium nitrates; potassium nitrate and sodium chloride; and sodium nitrate and potassium chloride; and the requisite dissociation constants have been derived (Part I, *Trans. Faraday Soc.*, 1927, **23**, 351): for potassium nitrate $K = 1{\cdot}3$, for sodium nitrate $K = 3{\cdot}8$, and the chlorides are completely dissociated. We shall expect that on mixing potassium nitrate and chloride in equimolecular amount there will occur a slight decrease in the extent of dissociation of the potassium nitrate, on account of the higher concentration of the common (potassium) ion in the added potassium chloride solution. A conductivity decrease slightly greater than would be expected from the very small mobility effect should therefore occur, and this is what is found; Van Rysselberghe and Nutting report a decrease of 0·3 unit, whilst the decrease predicted, on the basis of calculations outlined later, is 0·6 unit. The same arguments apply to the sodium nitrate–chloride mixture, but the effect should be smaller, as sodium nitrate is more fully dissociated than potassium nitrate; here the experimental decrease is 0·2 unit and the calculated decrease 0·2 unit. With potassium and sodium nitrates the adjustment on mixing is again small; the experimental decrease is 0·4, the calculated decrease 0·7.

With the remaining two mixtures much larger effects are to be anticipated owing to the absence of a common ion; moreover, they should be in opposite directions in the two cases, and therefore provide a good test of the theory of mass-action effects. On mixing potassium nitrate and sodium chloride solutions, adjustment to the new concentrations will involve the breaking up of a number of potassium nitrate ion-pairs with a consequent increase of conductivity; this will be only partly offset by the formation of sodium nitrate

ion-pairs, since sodium nitrate is the stronger salt, so that the net effect will be a marked increase in conductivity. With sodium nitrate and potassium chloride, on the other hand, the change will be a decrease in conductivity, since the association of potassium with nitrate ions will more than counterbalance the dissociation of sodium nitrate ion-pairs. These predictions are in complete agreement with Van Rysselberghe and Nutting's results, as will be seen from the following table, in which the experimental and calculated values of the deviations from additivity are compared :

| $KNO_3 + NaCl$. | | | $NaNO_3 + KCl$. | | |
|---|---|---|---|---|---|
| Molality. | $\Delta\Lambda$, expt. | $\Delta\Lambda$, calc. | Molality. | $\Delta\Lambda$, expt. | $\Delta\Lambda$, calc. |
| $0{\cdot}9NaCl, 0{\cdot}1KNO_3$ ......... | +0·5 | +0·7 | $0{\cdot}9KCl, 0{\cdot}1NaNO_3$ ......... | −1·0 | −1·3 |
| $0{\cdot}75NaCl, 0{\cdot}25KNO_3$ ...... | +1·2 | +1·5 | $0{\cdot}75KCl, 0{\cdot}25NaNO_3$ ...... | −2·4 | −2·6 |
| $0{\cdot}5NaCl, 0{\cdot}5KNO_3$ ......... | +1·8 | +1·8 | $0{\cdot}5KCl, 0{\cdot}5NaNO_3$ ......... | −2·9 | −3·5 |
| $0{\cdot}25NaCl, 0{\cdot}75KNO_3$ ...... | +1·2 | +1·3 | $0{\cdot}25KCl, 0{\cdot}75NaNO_3$ ...... | −2·3 | −2·5 |
| $0{\cdot}1NaCl, 0{\cdot}9KNO_3$ ......... | +0·6 | +0·6 | $0{\cdot}1KCl, 0{\cdot}9NaNO_3$ ......... | −1·1 | −1·2 |

The calculations at such high concentrations must necessarily involve a number of uncertainties. The most serious approximation made was to assume that the mean ionic activity coefficients remain constant throughout each series of mixtures, and the probable errors involved in this approximation are sufficient to cover the differences between $\Delta\Lambda$, expt. and $\Delta\Lambda$, calc. shown in the table. With this approximation the dissociation of potassium nitrate can be written $[K^{\cdot}][NO_3{}'] / [KNO_3] = K_0/f_{\pm}{}^2 = K'$, where $K'$ has a constant value for all mixtures of 1-molal total concentration, and similarly for sodium nitrate. $K'$ is determined as follows. Combination of MacInnes and Longsworth's value (*Chem. Reviews*, 1932, **11**, 210) for the transport number of 1N-potassium chloride with Van Rysselberghe and Nutting's conductivities gives the following ionic conductivities at 1N : $l_{K^{\cdot}} = 54{\cdot}7$, $l_{Na^{\cdot}} = 28{\cdot}8$, $l_{Cl'} = 57{\cdot}4$; Shedlovsky's mobilities at zero concentration for chloride, potassium, and nitrate ions are respectively : 76·3, 73·5, 71·4, and for the nitrate ion at 1N the value 52·7 may accordingly be taken. Curves of ionic conductivity against the square root of the concentration can now be constructed, Shedlovsky's figures up to 0·1N being combined with the values just derived, and a comparison between these and Van Rysselberghe and Nutting's experimental conductivities for 1-molal potassium and sodium nitrates enables the degree of dissociation in these two solutions to be calculated in the usual way by successive approximations. The values obtained are : $KNO_3$, $\alpha = 0{\cdot}855$, $K' = 4{\cdot}8$; $NaNO_3$, $\alpha = 0{\cdot}926$, $K' = 11{\cdot}5$. Some check on these values is obtained by comparing them with the $K_0$ values previously determined at low ionic strengths and so calculating $f_{\pm}$. This procedure gives, for potassium nitrate, $f_{\pm} = 0{\cdot}58$, which may be compared with the experimental value for potassium chloride, $f_{\pm} = 0{\cdot}61$; similarly for sodium nitrate, $f_{\pm} = 0{\cdot}64$, the experimental value for sodium chloride being 0·65. The values are therefore reasonable ones. The actual ionic composition of the mixtures can now be obtained by successive approximations, and the conductivity calculated on this basis can be compared with that calculated from the mixture rule to give $\Delta\Lambda$, calc. The following figures illustrate the process for 0·5-molal potassium chloride plus 0·5-molal sodium nitrate. The density of the solution is 1·0456, and therefore 1 l. contains 0·4842 equiv. of each component. $K'_{KNO_3} = 4{\cdot}8$, $K'_{NaNO_3} = 11{\cdot}5$, and by successive approximations the composition of the solution is given by : $[NaNO_3] = 0{\cdot}0174$, $[KNO_3] = 0{\cdot}0395$, $[Na^{\cdot}] = 0{\cdot}4668$, $[K^{\cdot}] = 0{\cdot}4447$, $[Cl'] = 0{\cdot}4842$, $[NO_3{}'] = 0{\cdot}4273$ mol./l. The specific conductivity is therefore given by : $1000\ \kappa_{calc.} = 0{\cdot}4668\ l_{Na^{\cdot}} + 0{\cdot}4447\ l_{K^{\cdot}} + 0{\cdot}4273\ l_{NO_3{}'} + 0{\cdot}4842\ l_{Cl'}$. The 1-molal sodium nitrate is 92·6% dissociated, and so the simple mixture rule would give : $1000\ \kappa_{mixt.} = 0{\cdot}4842 \times 0{\cdot}926\ (l_{Na^{\cdot}} + l_{NO_3{}'}) + 0{\cdot}4842\ (l_{K^{\cdot}} + l_{Cl'})$. Subtracting, $1000\ \Delta\kappa = 0{\cdot}0176\ l_{Na^{\cdot}} - 0{\cdot}0395\ l_{K^{\cdot}} - 0{\cdot}0219\ l_{NO_3{}'} = -2{\cdot}81$, and $\Delta\Lambda = -2{\cdot}81/0{\cdot}97 = -2{\cdot}9$. In addition, a conductivity decrease of approximately 0·6 unit is to be expected on account of the mobility effect, giving a total decrease of 3·5 units.

In a second paper, Van Rysselberghe, Grinnell, and Carlson (*loc. cit.*) report measurements on a number of mixtures containing bivalent ions. The majority of these are mixtures of an alkali metal halide with the corresponding halide of zinc or cadmium, and the authors are undoubtedly correct in attributing the large conductivity decreases to the formation of complex anions; the absence of the effect when the bivalent metal is magnesium is also what would be expected from the fact that magnesium chloride is completely dissociated (Righellato and Davies, *Trans. Faraday Soc.*, 1930, **26**, 592). With mixtures of cadmium sulphate and potassium sulphate, however, there is no necessity to

postulate the existence of complex ions to explain the conductivity decrease; potassium sulphate ($K = 0{\cdot}15$) is a much stronger electrolyte than cadmium sulphate ($K = 0{\cdot}0038$), and the decrease in conductivity will follow from the partial suppression of the dissociation of the cadmium sulphate, just as in the parallel cases of the chloride–nitrate mixtures already discussed.

Some further data suitable for the present discussion have been obtained by Smith and Gortner (*loc. cit.*), who investigated a large number of mixtures at 30·17°. For the binary combinations hydrochloric acid plus potassium chloride, and magnesium chloride plus sodium chloride, only small deviations from additivity were found, and this is in accordance with expectations, since the electrolytes are completely dissociated; for mixtures of copper and zinc sulphates the deviations were also small, which is explained (see below) by the fact that these salts, though weak, have identical dissociation constants (Part I, *loc. cit.*); these examples do not require further consideration. The remaining five combinations of salts showed large deviations, sometimes positive, sometimes negative, and in three cases changing sign with changes in the total concentration. The authors offered no explanation for "the apparently erratic behaviour of these conductivity measurements." These results will be considered in turn.

*For sodium chloride–sodium sulphate mixtures* the measured conductivities are 0·3 unit higher than the calculated (additive) values at total concentrations of 0·01 and 0·1N, but about 1·5 units lower than those calculated at 1·0 and 2·0N. The explanation is that two influences are at work, the one predominating in the more dilute solutions being a mobility effect that we have not previously had to consider. At 0·01N total concentration the ionic strength of the sodium chloride is 0·01, but that of the sodium sulphate is approximately 0·015. Here, therefore, as with every mixture of salts of different valency types, mixing will cause a large alteration of ionic strength, with a resulting change in the mobilities of all four ions. The largest of these changes will be that of the bivalent sulphate ion, and for this reason there will be a significant increase in the conductivity of the mixture. An approximate calculation based on Onsager's equation gives $\Delta\Lambda = +\,0{\cdot}4$ for the increase at 0·01N; at higher concentrations the value will be smaller. In addition to this mobility effect there is a small mass-action effect due to a depression of the dissociation of the $NaSO'_4$ ion; this amounts to only $-0{\cdot}06$ unit at 0·01N, but at higher concentrations will be greater. At 0·01N, therefore, the net calculated effect is $\Delta\Lambda = +\,0{\cdot}3$, in agreement with the experimental result. The calculations have not been taken to higher concentrations, where the inevitable approximations would lead to uncertainties of the order of magnitude of the small changes observed, but clearly the effects described are sufficient to explain the result at 0·01N and to account for the change of sign observed at higher concentrations.

*In mixtures of magnesium chloride and sodium sulphate* large decreases of conductivity are observed, the deviation from the mixture rule amounting to as much as 10% of the total conductivity in some cases. This is due to the formation of magnesium sulphate ion-pairs. In the following table observed and calculated values for the conductivity decrease at a total concentration of 0·00465M are compared. The calculated values are low by about 0·6 unit, or 0·5% of the total conductivity, a discrepancy probably covered by the experimental error, and by the fact that no correction was made by Smith and Gortner for the volume change on mixing.

| | | | |
|---|---|---|---|
| Ratio $MgCl_2/Na_2SO_4$ | 80 : 20 | 50 : 50 | 20 : 80 |
| $\Delta\Lambda$, obs. | −5·0 | −7·5 | −4·6 |
| $\Delta\Lambda$, calc. | −4·3 | −6·8 | −4·3 |

At 0·005M the calculations involve no undue approximations. The composition of each mixture is first calculated from the equations derived in previous papers (*loc. cit.*): $\log [Na^{\cdot}][SO_4''] / [NaSO_4'] = \log 0{\cdot}20 + 2\sqrt{I} - 1{\cdot}3I$, and $\log [Mg^{\cdot\cdot}][SO_4''] / [MgSO_4] = \log 0{\cdot}0061 + 4\sqrt{I} - 4I$; the conductivity is then calculated by means of ionic mobilities obtained from Smith and Gortner's data for the pure salt solutions, the cation transport number of potassium chloride being assumed to be the same at 30·17° as at 25°. No allowance has been made for the mobility effect, which at this concentration will be small.

With mixtures of magnesium chloride and magnesium sulphate a decrease in conductivity is again to be expected, since the dissociation of the magnesium sulphate will be depressed on account of the higher concentration of magnesium ions in the added solution. This is what is found, the observed and calculated changes at 0·005M being as follows:

| | | | |
|---|---|---|---|
| Ratio $MgCl_2/MgSO_4$ | 80 : 20 | 50 : 50 | 20 : 80 |
| $\Delta\Lambda$, obs. | −1·7 | −1·7 | −1·1 |
| $\Delta\Lambda$, calc. | −0·9 | −1·3 | −0·8 |

The other two combinations studied by Smith and Gortner were mixtures of sodium chloride with the sulphates of zinc and copper. Calculations regarding these mixtures must involve the dissociation constants of zinc and copper chlorides, which are not yet known with certainty. Conductivity measurements at 0·5N indicate (Banks, Righellato, and Davies, *Trans. Faraday Soc.*, 1931, **27**, 621) that both are highly dissociated, and unpublished calculations based on some solubility measurements of Peterson and Meyers (*J. Amer. Chem. Soc.*, 1930, **52**, 4853) support this conclusion for copper chloride. On the other hand, Riley and Smith (J., 1934, 1448) consider copper chloride to be one of the weakest of inorganic salts, and by a potentiometric method obtain for it the approximate dissociation constant $K = 0·0016$. The great discrepancy between these conclusions prompted a reconsideration of Riley and Smith's measurements, as a result of which it is believed that the effects observed by them were primarily due to the difference in ionic strength in the two sides of their concentration cell, and that this, together with the influence of various experimental difficulties, makes their estimate of the dissociation constant an unreliable one. In considering Smith and Gortner's results it has therefore been assumed that the dissociation of copper and zinc chlorides at 0·005N is complete, an approximation that is not likely to cause very serious errors. The main result of mixing copper or zinc sulphate with sodium chloride will then be an increase in conductivity due to the dilution of the metal sulphate and the resulting increase in its degree of dissociation, and this will be only slightly offset by the much smaller interaction between the sodium and sulphate ions. The calculated increase is the same for zinc as for copper sulphate, since the dissociation constants of the two are identical. The observed and calculated values at 0·01N concentration are as follows:

| | | | |
|---|---|---|---|
| Ratio $NaCl/XSO_4$ | 80 : 20 | 50 : 50 | 20 : 80 |
| $\Delta\Lambda$, obs. ($ZnSO_4$) | +4·5 | +5·1 | +3·3 |
| $\Delta\Lambda$, obs. ($CuSO_4$) | +4·0 | +5·6 | +2·6 |
| $\Delta\Lambda$, calc. | +3·7 | +5·3 | +2·7 |

It may be noticed that with this type of mixture, unlike those previously considered, the magnitude of the measured change depends markedly upon which constituent is in excess; and that this peculiarity also is faithfully reproduced by the calculated figures.

With these two salt mixtures Smith and Gortner found that at higher concentrations the conductivity increase diminishes, and at 2N is replaced by a decrease. This is most probably due to the formation of complex anions by the chloride ion and the bivalent metal (compare Van Rysselberghe, Grinnell, and Carlson's results for zinc iodide–potassium iodide mixtures). At 0·01N this will be quite negligible, and the conductivity change, as we have seen, is mainly due to the dissociation of the bivalent metal sulphate; but it follows from the mass-action law that as the concentration is increased the latter effect becomes less, whereas the formation of complex anions becomes more and more, important. The net effect will therefore be a change in the sign of $\Delta\Lambda$ such as is actually observed.

To summarise this discussion: in every recorded case where the conductivity change on mixing two salt solutions cannot be explained by mobility changes, the results are in the direction and, within the limits imposed by the uncertainties of the calculations, are of the magnitude to be predicted on the basis of the known dissociation constants. The conductivity change is greatest when an incompletely dissociated electrolyte is mixed with a highly dissociated electrolyte not containing a common ion, and experiments with such mixtures may well prove valuable in detecting incomplete dissociation or in providing

approximate confirmation of dissociation constants found by other methods. In such measurements the change observed in the equivalent conductivity will of course depend on the concentration range employed, but the choice of concentration is not critical. For instance, the bivalent metal sulphates ($K = ca.$ 0·005) will exhibit the maximum conductivity increase at $M = 0{\cdot}01$, approximately, but the increase will still be 75% of the maximum at concentrations of 0·0025 or 0·04M.

Finally, there is a general case which calls for treatment. When equimolecular solutions of two electrolytes of the same valency type, and with identical, or almost identical, dissociation constants are mixed, there will be no measurable departure from the mixture rule, provided they possess an ion in common. This statement is easily justified by an extension of the isohydric principle. For both salts before mixing we can write $\alpha^2 m/(1 - \alpha) = K/f_{\pm}^2$, where $f_{\pm}$ is the mean ion activity coefficient. Now it has been shown in previous papers (compare Banks, Righellato, and Davies, *loc. cit.*) that the deviations observed amongst the stoicheiometric activity coefficients of salts of any given valency type can, in dilute solution, be attributed entirely to the mass-action effects, and that the mean ion activity coefficients at a given ionic concentration are identical. If $K$, in the equation just given, is also the same for the two salt solutions, these must before mixing have the same degree of dissociation. After the two salts have been mixed in the ratio $x : (1 - x)$, the equations for them become $x\alpha^2 m/x(1 - \alpha) = K/f_{\pm}^2$ and $(1 - x)\alpha^2 m/(1 - x)(1 - \alpha) = K/f_{\pm}^2$; clearly no change is demanded in the degree of dissociation or the ionic strength, and there will be no departure of the conductivity from additivity except in so far as there is a mobility effect. Two examples of this kind have been studied by O'Connor (*loc. cit.*), who measured the conductivities of very dilute solutions of the sulphates and dithionates of calcium and strontium. He found that the conductivities of all four salts, when plotted against the square root of the concentration, give slopes far greater than those derived from Onsager's equation; that calcium and strontium sulphate show identical conductivities throughout the range of concentrations examined, and that the same is true of the dithionates. He then investigated mixtures of the two sulphates, and also of the two dithionates, and found the conductivities of these to be additive, which result, he states, indicates complete dissociation of the salts. It will be seen, however, that if we attribute the deviations from Onsager's equation to incomplete dissociation we must assign identical dissociation constants to calcium and strontium sulphates, since their conductivity curves are identical throughout, and that therefore there can be no alteration in the degree of dissociation on mixing solutions of the same concentration. Furthermore, since the mobilities of calcium and strontium are found to be the same, there will be no mobility effect. The conductivities of all mixtures of the two salts will necessarily be additive therefore, and the fact can afford no evidence for complete dissociation. The same is true of the dithionates.

If the two salts, say CA and KS, have identical dissociation constants but no common ion, the mixed conductivity will clearly depend on the dissociation constants of the salts formed, CS and KA, and on the mobilities of the ions no longer free to conduct. If all four salts have identical dissociation constants, however, it is easy to show that the mixed conductivity is once more additive. Though this condition is not likely to be exactly fulfilled in any actual mixture, it will quite commonly be approximately fulfilled, and the conductivity changes to be looked for in such cases will be very small.

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# 90. *The Solvent Factor in Catalytic Hydrogenation.*

By EDWARD B. MAXTED and VICTOR STONE.

*An attempt is made to correlate velocity of hydrogenation with properties of the solvent such as viscosity or solvent power for hydrogen. Even when the partial pressure of hydrogen is corrected for that due to the solvent vapour, the specific velocity shows no simple relation to the above properties. The solvents were treated so as to secure removal of possible catalyst poisons.*

THE variation in the velocity of the catalytic hydrogenation of a dissolved substance with the solvent is of interest in connection with the resolution of the total hydrogenation process into its component stages, since the rate of supply of dissolved hydrogen at the catalysing surface is determined in such cases by its rate of passage from the gas phase through the solvent. On reviewiug the literature, instances were observed in which the hydrogenation velocity is reported to vary widely with the nature of the solvent employed. For instance, Willstätter and Hatt (*Ber.*, 1912, **45**, 1471) found that the hydrogenation of naphthalene took place three times as rapidly in glacial acetic acid as in ether; and Kelber and Schwarz (*ibid.*, p. 1946), in order to allow hydrogenation to be carried out in acetic acid with colloidal metallic catalysts, prepared colloidal palladium in the presence of a protective colloid stable in acids.

It has accordingly been considered of interest to re-examine the solvent factor with a number of organic solvents which had previously been carefully purified from any trace of catalyst poisons, since it appeared conceivable that any observed differences might, at least to some degree, be due to the presence of small quantities of inhibitants rather than to specific solvent action. The solvents investigated included alcohol, ether, ethyl acetate, acetic acid, *cyclo*hexane, and chloroform; and the results of the work indicate that, although reaction in acetic acid takes place slightly faster than in the other media, this difference is considerably less than that given above: indeed, if a correction be made for the decreased partial pressure of hydrogen, due to the vapour pressure of the solvent, reaction takes place more quickly in ethereal solution than in acetic acid.

The system hydrogenated consisted in each case of 1 g. of crotonic acid, which was taken as a convenient unsaturated substance, together with 9 c.c. of the solvent and 0·1 g. of a standard preparation of non-colloidal platinum containing 0·0085 g. of metal. Hydrogenation was carried out in a mechanically driven shaker under standard conditions in the ordinary manner, the temperature being 20° in every case. All substances employed, including the crotonic acid, were freed from poisons by being previously allowed to remain in contact with a large excess of active platinum or nickel, from which they were subsequently separated by filtration, followed by redistillation. The relative velocities of hydrogenation in the various purified solvents are given in the table, $k$ being the rate expressed in c.c. per minute. The reaction course in these poison-free solvents was very nearly of zero order up to an advanced stage of saturation.

| Solvent. | $k$. | $k$, corrected for vapour pressure of solvent. | Solubility of hydrogen, $\alpha_{20°}$. | Viscosity of solvent, $100\,\eta_{20°}$. |
|---|---|---|---|---|
| Acetic acid | 18·7 | 19·0 | 0·0563 | 1·24 |
| Ethyl acetate | 17·7 | 19·6 | 0·0758 | 0·45 |
| Chloroform | 15·2 | 19·3 | 0·0596 | 0·56 |
| Ethyl alcohol | 14·1 | 15·0 | 0·0766 | 1·72 |
| *cyclo*Hexane | 11·6 | 12·9 | — | 0·96 |
| Ethyl ether | 11·2 | 26·8 | 0·118 | 0·23 |

The concentration of the dissolved hydrogen in the solvent will be a function of the partial pressure of hydrogen in the gas phase and of the solubility coefficient; and, in addition, the rate of transport of the gas from the gas phase, through the solvent, to the catalytic surface will vary with the viscosity and with other factors which determine the rate of diffusion or mixing: accordingly, the respective values for $\alpha$, the Bunsen solubility coefficient for hydrogen, at 20°, in the solvent in question, and for the viscosity of the solvent, $\eta$, in poises, have also been inserted in the table. It has been found that, for a given liquid, the hydrogenation velocity varies approximately linearly with at any rate small

variations in the hydrogen pressure (*J. Soc. Chem. Ind.*, 1921, **40**, 169T), and it is consequently possible to correct for the partial pressure of the hydrogen, as has been done in col. 3 of the table; but the quantitative influence of the other factors, *i.e.*, the solubility coefficient and the viscosity, is not known sufficiently to justify the insertion of the appropriate corrections. It seems justifiable to assume, however, a saturated hydrogen–solvent layer at the gas–liquid interface, the hydrogen concentration in which is proportional to the solubility at the partial pressure in question and from which the rate of transport of dissolved gas to the catalyst—both by diffusion and by mechanical mixing—is facilitated by a decrease in the viscosity.

It will be seen that, after correction of the hydrogen pressure for the partial pressure of solvent vapour in the gas phase, there is little difference in the rate in acetic acid, ethyl acetate, or chloroform. The somewhat lower rate in ethyl alcohol may to some degree be due to the high value of the viscosity, and the higher corrected velocity in ether to the higher hydrogen solubility and lower viscosity; but any regular variation in rate on the basis of solubility and viscosity is at the best only very approximate: for instance, chloroform, with its considerably lower viscosity and approximately equal hydrogen solubility, compared with acetic acid, gives very nearly the same corrected hydrogenation velocity as that obtained in the latter solvent.

UNIVERSITY OF BRISTOL. [*Received, March 5th*, 1938.]

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## 91. *Catalytic Toxicity and Chemical Structure. Part III. The Influence of Various Factors on the Toxicity of Sulphur Compounds.*

By EDWARD B. MAXTED and HERBERT C. EVANS.

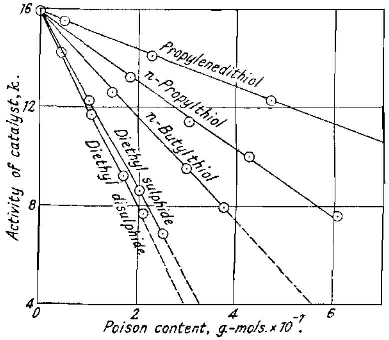
The principal point of interest in the present work is that the addition of a second terminal sulphur atom to a hydrocarbon chain of given length decreases rather than increases the toxicity per g.-mol. It is considered that this is due to the restriction imposed on the mobility, since the decrease in toxicity does not occur if the sulphur atoms are adjacent to one another.

IN Parts I and II (J., 1937, 603, 1004), the development of toxic properties in normally non-toxic hydrocarbon chains by enforced proximity to a catalytic surface—by virtue, for instance, of the permanent attachment of one end of the chain to the surface by a terminal sulphur atom—has been examined for hydrocarbon chains of various lengths.

A point of considerable interest arises if the hydrocarbon chain contains two terminal sulphur atoms in place of one. In the case of a single sulphur anchor, the chain as a whole is free, save for its permanent attachment at one end; and the maximum surface area over which there is a time-probability of adsorption is a circle of radius equal to the chain length. It should be possible, however, to restrict this mobility, and consequently to diminish the area of influence, by providing a second sulphur anchor at the other end of the chain, in a manner analogous to the effect of two anchors, in place of oue, in restricting the area of possible drift of a boat. Accordingly, if the explanation of induced toxicity which has been developed in previous papers is correct, the molecular toxicity of a hydrocarbon-chain compound terminated at each end by a catalytically poisonous element or group should, in spite of its possessing twice the content of sulphur or other poisonous element, be considerably less than that of a chain of similar length containing only a single terminal sulphur atom. This point has now been verified experimentally, in that the molecular toxicity of propylenedithiol, $SH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}SH$, was found, in spite of its greater sulphur content, to be considerably less than that of either *n*-propylthiol, $CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}SH$, or of *n*-butylthiol, $CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}SH$, with which latter compound the dithiol is perhaps more nearly comparable from the standpoint of chain length owing to the inclusion of the extra sulphur atom. If, on the other hand, the two sulphur atoms, instead of occupying terminal positions, are adjacent to one another, little change in toxicity would be expected: thus, diethyl disulphide, $(C_2H_5)_2S_2$, does not differ greatly

in molecular toxicity from diethyl sulphide, $(C_2H_5)_2S$, again in spite of its doubled sulphur content. The relevant data are given in Table I.

Other points which have been investigated include the effect of a double bond and of a branching chain. It would perhaps be expected that a hydrocarbon chain, anchored to a surface at one end and containing an unsaturated bond, would be less toxic than a compound containing a saturated chain of equal length, by reason of the probable greater adsorbed life, and consequently the lesser mobility, of the unsaturated group, accompanied by a less effective cover of the total surface within the range of the chain. The inclusion of a double bond was, however, found on trial to have little influence on the poisoning power, in that there is little difference between the molecular toxicity of *n*-propyl and of allyl sulphide. The relative toxic effectiveness of an anchored branching hydrocarbon chain, compared with that of a straight chain containing the same number of carbon atoms, has been studied for *n*-propyl and *iso*propyl sulphides. Here the normal chain, probably by reason of its greater length, is somewhat more toxic than the *iso*-compound; but the difference is not great. It is probable that the restriction in the range brought




about by the shorter chain is not compensated by the greater effectiveness of cover which would be expected within this restricted range by virtue of the greater area of the chain ends. The relative toxicities are shown in Table II.

Measurements were also made of the toxic effect of an anchored hydrocarbon ring, in place of a chain. Three cases, representing progressive stages in the removal of the ring from the poisonous atom proper, were examined, *viz.*, thiophen, in which the sulphur anchor is contained in the ring itself, thiophenol, in which it is adjacent to this, and β-phenylethylthiol, $C_6H_5{\cdot}CH_2{\cdot}CH_2{\cdot}SH$, in which the ring is connected with the anchor by means of a short chain. Thiophenol, as would be expected from its six- in place of five-membered ring, together with its increased range by virtue of the extra-cyclic sulphur atom, was more toxic than thiophen; but β-phenylethylthiol—probably by reason of the greater distance of removal of the benzene ring from the catalyst surface and consequently the less favourable position of the ring for preferential adsorption—showed an effective toxicity intermediate between those of thiophen and thiophenol (see Table III).

Finally, some work was done on the toxicity of substituted thioureas and certain related substances. This group seemed at first sight an easily obtained series, in which the influence of chain length and molecular complexity could be studied in a similar manner to that already carried out for long-chain thiols and sulphides. Unfortunately, however, the thioureas are capable of ready isomerisation; and there is difficulty in determining the isomeric form or forms in which the poison is acting.

## EXPERIMENTAL.

The general technique and the method of expressing toxicity were as described in previous papers and are not repeated here. A uniform stock of supported platinum was used throughout, and the standard reaction employed for measuring the activity of the catalyst at various stages of poisoning was, as before, the hydrogenation of crotonic acid at 27°. Each charge consisted of 5 c.c. of 2N-crotonic acid in acetic acid solution, to which was added a further 5 c.c. of acetic acid containing a known quantity of poison, and 0·05 g. of the standard catalyst.

*Influence of a Second Sulphur Atom.*—The poisoning graphs for *n*-propylenedithiol, *n*-propylthiol and *n*-butylthiol under similar conditions are summarised in the figure, and the results show the relationship described on p. 455. With a hydrocarbon chain containing two terminal sulphur atoms, full extension across the catalytic surface is not probable, the mean occurring position being probably that in which the terminal sulphur anchors are attached in positions such that the chain is in a state of least strain; and rotary movement of the chain loop thus formed, about a horizontal axis passing through the terminal sulphur atoms, should be possible, the range of possible obstructive cover of potential adsorbing surface being however far less than for a chain of similar length anchored at one end only.

On calculating the values of $\alpha$ by means of the expression, $k_c = k_0 (1 - \alpha c)$, the values given in Table I are obtained.

TABLE I.

| Inhibitant. | $\alpha \times 10^{-5}$. | Rel. toxicity per g.-mol. of inhibitant. | Inhibitant. | $\alpha \times 10^{-5}$. | Rel. toxicity per g.-mol. of inhibitant. |
|---|---|---|---|---|---|
| *n*-Propylthiol ......... | 8·7 | 0·65 | Diethyl sulphide ...... | 22·7 | 1·00 |
| *n*-Butylthiol ............ | 13·3 | 1·00 | Diethyl disulphide ... | 25·0 | 1·10 |
| Propylenedithiol ...... | 5·1 | 0·38 | | | |

*Propyl,* iso*Propyl, and Allyl Sulphides.*—

TABLE II.

| Inhibitant. | $\alpha \times 10^{-5}$. | Rel. toxicity per g.-mol. of inhibitant. |
|---|---|---|
| *n*-Propyl sulphide ................................ | 19·8 | 1·00 |
| Allyl sulphide .................................... | 20·6 | 1·04 |
| *iso*Propyl sulphide .............................. | 17·6 | 0·89 |

*Miscellaneous Ring Compounds.*—The relative toxicities of these compounds are given in Table III.

TABLE III.

| Inhibitant. | $\alpha \times 10^{-5}$. | Rel. toxicity per g.-mol. of inhibitant. |
|---|---|---|
| Thiophen ...................................... | 9·9 | 1·00 |
| Thiophenol ...................................... | 16·1 | 1·63 |
| $\beta$-Phenylethylthiol .......................... | 12·0 | 1·21 |

An interesting case of unexpected toxicity was given by $\beta$-thionaphthol, which showed a toxicity only approximately equal to that of thiophenol ($\alpha \times 10^{-5} = 15·1$, on the same scale as in Table III). This was checked by duplicate determinations both with thiophenol and with thionaphthol. It is possible that this seeming anomaly, which is the first that has been encountered, may be due to the lesser mobility of the larger ring system, this factor compensating—from the standpoint of the degree of effectiveness of obstructive cover of the total surface within range—for the certainly greater maximum range of the larger ring.

*Toxicity of Derivatives of Thiourea.*—Owing to the possibilities of isomerism in these compounds, the observed effective toxicity, unlike that of stable poisons such as those previously studied (the toxicities of which are independent of the solvent used), changes with the conditions and with the solvent. It was not considered worth while in such cases to investigate further the conditions of equilibrium between possible products, since, from the present standpoint, a definite molecular form is desirable for correlation with the toxicity; and the figures in Table IV are merely given for purposes of record, as an indication of the effective toxicity exerted at 27° in acetic acid and in alcoholic solution respectively. It will be seen that only thioacetamide appears to retain its structure, and consequently has the same toxicity, in acetic acid and in alcohol.

TABLE IV.

| Inhibitant. | $\alpha \times 10^{-5}$. In HOAc. | $\alpha \times 10^{-5}$. In EtOH. | Relative effective toxicity per g.-mol. of inhibitant ($H_2S$ = 1). In HOAc. | Relative effective toxicity per g.-mol. of inhibitant ($H_2S$ = 1). In EtOH. |
|---|---|---|---|---|
| Thiourea | 13·5 | 20·5 | 5·9 | 9·0 |
| *s*-Diphenylthiourea | 16·6 | 25·1 | 7·3 | 11·1 |
| *s*-Diphenylthiocarbazide | 26·5 | 15·9 | 11·7 | 7·0 |
| Thiosinamine | 7·3 | 18·4 | 3·2 | 8·1 |
| Thioacetamide | 8·3 | 8·25 | 3·66 | 3·64 |

UNIVERSITY OF BRISTOL.

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## 92. *Kationoid Reactivity of Aromatic Compounds. Part V. Fission of Arylsulphones by Means of Sodamide and Piperidine.*

By WILLIAM BRADLEY.

Simple arylsulphones undergo fission when treated with a mixture of sodamide and piperidine with formation of an *N*-arylpiperidine and a sulphinic acid. No replacement of nuclear hydrogen by the piperidino-group is observed even when the reaction is carried out in presence of oxygen.

IN previous work (Bradley and Robinson, J., 1932, 1254; Bradley, J., 1937, 1091) it has been shown that replacement of nuclear hydrogen by the piperidino-group may occur in aromatic nitro- or carbonyl compounds when these are treated with sodamide and piperidine. When the same reagents are applied to simple arylsulphones, no substitution is observed even when oxygen is present, but fission takes place with formation of an *N*-arylpiperidine and a sulphinic acid :

$$NaNH_2 + NHC_5H_{10} = NH_3 + NaNC_5H_{10}$$
$$^{-}NC_5H_{10} + Ar{\cdot}SO_2R = Ar{\cdot}NC_5H_{10} + R{\cdot}SO_2^{-}$$

Diphenylsulphone, phenylbenzylsulphone, and *p*-tolylmethylsulphone are all readily decomposed at the boiling point of piperidine. Diphenylsulphone gives *N*-phenylpiperidine in 75% of the theoretical yield and benzenesulphinic acid, the latter in almost pure condition; phenylbenzylsulphone affords *N*-phenylpiperidine and benzylsulphinic acid; *p*-tolylmethylsulphone gives *N*-*p*-tolylpiperidine and methylsulphinic acid. Methylsulphinic acid was characterised as methylbenzylsulphone (Fromm and de Seixas Palma, *Ber.*, 1891, **24**, 3315). That the Alkyl·$CH_2$·$SO_2$ link is more resistant to fission than is the Aryl·$SO_2$ is substantiated further by the stability of dibenzylsulphone, which was recovered almost unchanged after heating with piperidine and a large excess of sodamide.

The reaction is thus one of a class which includes the formation of amines from sulphonic acids by heating these with sodamide at 230° (Sachs, *Ber.*, 1906, **39**, 3009; cf. Jackson and Wing, *Ber.*, 1886, **19**, 902), and the conversion of sulphonic acids into phenols by fusion with alkali hydroxides. A distinguishing feature of the present reaction is the ease with which it takes place.

The direction of fission in substituted arylalkylsulphones may be determined by the nature of the substituent. An electron-donating group (*e.g.*, OH, $NH_2$) present in the side chain of an arylalkylsulphone does not affect the normal direction of fission. On the other hand, electron-attracting groups (*e.g.*, $SO_2$, CN) may cause reversal of the normal direction of fission, the aryl group appearing as a sulphinic acid, and the substituted alkyl group in combination with the reagent. Ethylenebis-*p*-tolylsulphone and aqueous potassium hydroxide afford *p*-toluenesulphinic acid and β-*p*-tolylsulphonylethyl alcohol (Otto, *J. pr. Chem.*, 1884, **30**, 355). Ethylenebisphenylsulphone similarly gave β-phenylsulphonylethyl alcohol and benzenesulphinic acid, but prolonged heating with concentrated alkali failed to hydrolyse the sulphone alcohol (Otto, *ibid.*, p. 321). The same mode of fission was observed when the reagent was ammonia or potassium hydrosulphide. When

potassium cyanide was used, however, the intermediate cyano-substituted sulphone was further changed to succinonitrile and succinic acid (Otto, *ibid*, pp. 349, 361).

$$Ar{\cdot}SO_2{\cdot}CH_2{\cdot}CH_2{\cdot}SO_2Ar \xrightarrow{KOH} Ar{\cdot}SO_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH + Ar{\cdot}SO_2K$$

$$\downarrow KCN$$

$$(Ar{\cdot}SO_2{\cdot}CH_2{\cdot}CH_2{\cdot}CN) + Ar{\cdot}SO_2K \xrightarrow{KCN} Ar{\cdot}SO_2K + CN{\cdot}CH_2{\cdot}CH_2{\cdot}CN$$

## Experimental.

*Fission of Diphenylsulphone.*—Sodamide (15 g.) was boiled with piperidine (50 c.c.) during 15 minutes and then diphenylsulphone (25 g.) was added to the suspension. There was a rapid evolution of ammonia. The mixture was boiled for 2 hours under reflux, benzene (300 c.c.) added, and then water (75 c.c.) portionwise and with frequent shaking.

The benzene layer, washed with water and dried over potassium hydroxide, gave on distillation a fraction (13·5 g.), b. p. 255—260°/766 mm., which was almost pure *N*-phenylpiperidine. The pure base had b. p. 259°/766 mm.; the picrate crystallised from alcohol in bright lemon-yellow prisms, m. p. 148° (Found: N, 15·0. Calc. for $C_{17}H_{18}O_7N_4$: N, 15·0%). von Braun (*Ber.*, 1904, **37**, 3212; 1907, **40**, 3920) gives b. p. 257—258°/752 mm. and m. p. 148°, respectively.

The alkaline aqueous solution was filtered, cooled in ice, and acidified. An oil separated which quickly solidified. Dried on porous tile, the crude product had m. p. 83°; benzenesulphinic acid has m. p. 83—84° (Otto, *loc. cit.*). When the crude sulphinic acid (7 g.) was heated during 1·5 hours with benzyl chloride (6·5 g.) and a solution of potassium hydroxide (3 g.) in alcohol (30 c.c.), phenylbenzylsulphone (9·5 g., m. p. 148°) was obtained (cf. Knoevenagel, *Ber.*, 1888, **21**, 1695).

p-*Acetamido*-N-*phenylpiperidine.* 6·5 G. of *N*-phenylpiperidine obtained by fission of diphenylsulphone were dissolved in concentrated hydrochloric acid (20 c.c.), the solution cooled to 0° by addition of ice, and a concentrated aqueous solution of sodium nitrite (3 g.) added through a capillary tube with frequent shaking. The solution, at first colourless, became intensely orange-yellow. It was filtered after 30 minutes, and concentrated hydrochloric acid (20 c.c.) added. The heated solution was decolourised with zinc dust (12 g.), cooled, and made alkaline in presence of ether. The ethereal solution was separated, washed with water, mixed with acetic anhydride (20 c.c.), and then evaporated on the water-bath. An oil remained and this was dissolved in alcohol, 5 c.c. of 10% sulphuric acid were added, and the solution kept overnight and then made alkaline. The grey crystalline precipitate was recrystallised from alcohol, giving colourless prisms, m. p. 151—152°, not depressed by *p*-acetamido-*N*-phenylpiperidine obtained from *p*-chloronitrobenzene (Lellmann and Geller, *Ber.*, 1888, **21**, 2286).

p-*Chlorobenzeneazo*-N-*phenylpiperidine.* The diazonium salt prepared from *p*-chloroaniline (2·5 g.) was added to a solution of *N*-phenylpiperidine (3·2 g.) in 5% hydrochloric acid (20 c.c.). A golden-yellow solution was formed, from which sodinm acetate (5 g.) precipitated a yellow oil. The *product* solidified and then crystallised from alcohol in golden-yellow plates, m. p. 143° (Found: N, 14·3. $C_{17}H_{18}N_3Cl$ requires N, 14·0%).

When oxygen was passed through a stirred suspension of sodamide (10 g.) in a solution of diphenylsulphone (25 g.) in piperidine (50 c.c.) which was kept for 1 hour at 118—120°, 7 g. of *N*-phenylpiperidine were obtained.

*Fission of* p-*Tolylmethylsulphone.*—The pure sulphone (7 g.) (Baldwin and Robinson, J., 1932, 1448) and sodamide (5 g.) were added to piperidine (20 c.c.) and gently boiled during 2 hours. Ammonia was evolved almost at once and a brown pasty mass formed. Benzene (50 c.c.) was added and then water (30 c.c.) portionwise.

The pale amber benzene layer was washed with water and dried over potassium hydroxide. On distillation, after benzene and piperidine had passed over, all but a small residue boiled at 274°/763 mm. (5·5 g.). According to von Braun (*loc. cit.*) *N*-*p*-tolylpiperidine has b. p. 268—269°; Lellmann and Just (*Ber.*, 1891, **24**, 2099) state b. p. 262°. The picrate crystallised when the base was added to 10% alcoholic picric acid. It formed bright yellow prisms, m. p. 176° (Found: N, 14·3. $C_{18}H_{20}O_7N_4$ requires N, 14·4%), not depressed by the picrate of *N*-*p*-tolylpiperidine prepared by Lellmann and Just's method.

The alkaline aqueous layer was colourless. When acidified with acetic acid, it decolourised iodine. When it was boiled for 1 hour with benzyl chloride (7 g.), and the solution cooled, an oil was precipitated which rapidly crystallised. After being pressed on porous tile, it separated

from alcohol in needles, m. p. 126°, not depressed by benzylmethylsulphone prepared by methylating benzylsulphinic acid (Fromm and de Seixas Palma, *Ber.*, 1906, **39**, 3319).

*Fission of Phenylbenzylsulphone.*—Sodamide (3 g.) was boiled for 15 minutes with piperidine (20 c.c.), the resulting suspension cooled to 90°, and phenylbenzylsulphone (8·5 g., m. p. 148°) added. There was an immediate reaction in which ammonia was evolved and a solid separated. After 30 minutes' boiling, benzene (50 c.c.) was added and then water (50 c.c.) in small successive amounts.

From the benzene solution there crystallised 3·5 g. of unreacted sulphone, and from the filtered solution *N*-phenylpiperidine, b. p. 255—260°, was obtained. The base afforded 2 g. of the picrate, m. p. 148°.

The alkaline aqueous layer, washed with benzene and then boiled for 1 hour with benzyl chloride (5 g.), gave dibenzylsulphone, which crystallised from alcohol in plates, m. p. 150—151°, not depressed by a specimen prepared by the benzylation of benzylsulphinic acid (Fromm and de Seixas Palma, *loc. cit.*).

*Non-fission of Dibenzylsulphone.*—The pure sulphone (0·5 g.) was boiled for 1·5 hours with piperidine (10 c.c.) and sodamide (1 g.). The reddish-brown solution obtained, when cooled and diluted with water, gave 0·43 g. of unchanged dibenzylsulphone. In a second experiment 1·5 g. of the sulphone were boiled for 3 hours with piperidine (15 c.c.) and sodamide (3 g.); 1·15 g. of unchanged sulphone were recovered.

College of Technology, Manchester. [*Received, March 1st, 1938.*]

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## 93. *Solvent Effect in Dielectric Polarisation. Part III. The Behaviour of Ethyl Alcohol in Certain Ethers.*

By George Thomson.

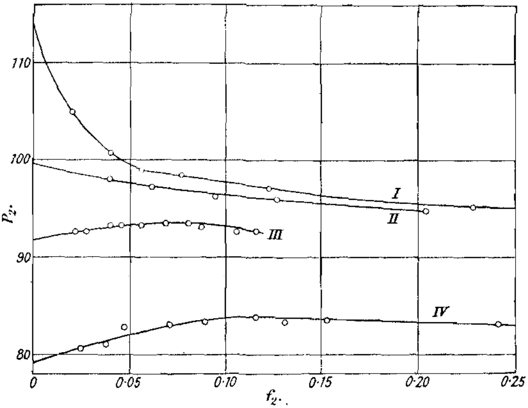
The polarisation of ethyl alcohol has been measured in *iso*propyl, *n*-butyl, and amyl ethers and in dioxan. The high values of polarisation at infinite dilution and the variation of polarisation with concentration are explained by formation of a hydrogen bond between the ether and the alcohol. Evidence in support of this view is adduced from cryoscopic measurements in other ethers.

The dielectric behaviour of the alcohols is of interest because, in non-polar solvents, the polarisation–concentration curves differ from those of other solutes in that they exhibit a maximum and not infrequently a minimum as well (cf., *inter alia*, Debye, "Handbuch der Radiologie," 1925, **6**, 635; Lange, *Z. Physik*, 1925, **33**, 169; Krchma and Williams, *J. Amer. Chem. Soc.*, 1927, **49**, 2408; Stranathan, *Physical Rev.*, 1928, **31**, 653; Smyth and Stoops, *J. Amer. Chem. Soc.*, 1929, **51**, 3312, 3330; Wolf and Herold, *Z. physikal. Chem.*, 1934, *B*, **27**, 58; Hoecker, *J. Chem. Physics*, 1936, **4**, 431).

In continuance of an investigation of the use of the aliphatic ethers as solvents in dielectric-polarisation measurements (Part I, J., 1937, 1051; Part II, *ibid.*, p. 1056), the polarisation of ethyl alcohol has been measured in di*iso*propyl, di-*n*-butyl, and diamyl ethers. The polarisation–concentration curves obtained are shown in Fig. 1, those for the last two solvents being of a different type from that in the first. High values are obtained in each case for the polarisation of the alcohol at infinite dilution: in *iso*propyl ether 91·9, in *n*-butyl ether 99·5, and in amyl ether 112. The polarisation of ethyl alcohol in the liquid state at 25° is 52·1 (Williams, *loc. cit.*), and in the vapour state at 25°, 72·4 (calculated from the data of Knowles, *J. Physical Chem.*, 1932, **36**, 2554). The exaltation of polarisation shown in solution in the ethers is too great to be accounted for simply by change in dielectric constant of solvent, and in any case is opposite in sign to the ordinary "solvent effect"; the alcohols are expected to show a polarisation increasing with increasing dielectric constant of the solvent (Higasi, *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1936, **28**, 284), though this effect is expected by Frank (*Proc. Roy. Soc.*, 1935, *A*, **152**, 171) to be small if, in fact, detectable. Hoecker (*loc. cit.*), working with extremely dilute solutions, found for ethyl alcohol at 24·5° in benzene $P_2 = 73{\cdot}16 \pm 0{\cdot}42$, and in carbon tetrachloride $P_2 = 71{\cdot}31 \pm 0{\cdot}33$. The value found by Knowles (*loc. cit.*) for the

vapour at this temperature was 72·8. There is general agreement that the shape of the polarisation curves for alcohols in non-polar solvents is due to association of the alcohol molecules, and Sidgwick (*Z. Elektrochem.*, 1928, **34**, 450) has suggested as the mechanism of association the formation of co-ordinate links between alcohol molecules, the oxygen of one molecule acting as donor and the hydroxylic hydrogen of another as acceptor. (For a modification of this in accordance with current theories, see Sidgwick, *Ann. Reports*, 1934, **31**, 41.) It seems probable that the behaviour of ethyl alcohol in the ethers is to be explained by the formation of a hydrogen bond between the ether and the alcohol $R_2O$ . . . . HOR, the polarisation–concentration curves showing this effect superimposed on that due to co-ordination between the alcohol molecules. The latter effect should increase with increasing alcohol concentration, the former with increasing ether concentration. The capacity of the ethereal oxygen to form a hydrogen bond should be increased by the attachment to it of more strongly electron-repelling groups and would therefore be expected

Fig. 1.




*Ethyl alcohol in :* I, *amyl ether ;* II, iso*butyl ether ;* III, iso*propyl ether ;* IV, *dioxan.*

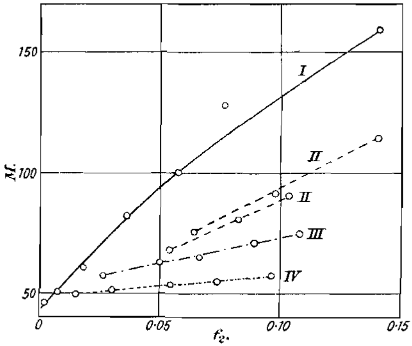
to increase with lengthening of the alkyl radical. Earp and Glasstone (J., 1935, 1709) found that the formation of complexes with chloroform and bromoform proceeded more readily with *iso*propyl ether than with ethyl ether, and as a rough analogy the ionisation constants of the aliphatic secondary amines increase in the order diethylamine < di*iso*-propylamine < di-*n*-butylamine (Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3469). No data are available for di-(β-methylbutyl)amine. (The amyl ether used seems to consist for the most part of the active ether.)

The propensity of dioxan to form molecular compounds is well known (cf. Rheinboldt and co-workers, *J. pr. Chem.*, 1931, **129**, 268, 273; 1932, **133**, 284), and Wilson and Wenzke (*J. Chem. Physics*, 1934, **2**, 546) have shown, from polarisation measurements, its efficacy in breaking down the dimers of acetic and propionic acids into simple molecules. Piperazine, the base corresponding to dioxan, has a lower dissociation constant than any of the aliphatic bases mentioned above, and it was therefore of interest to investigate the dielectric behaviour of ethyl alcohol in dioxan solution. The polarisation–concentration curve (Fig. 1) shows a maximum more pronounced than that obtained in *iso*propyl ether, and the value (79·2) of the polarisation at infinite dilution is lower.

*Evidence from other physical properties for formation of a hydrogen bond is, in the case of these solutions, difficult to obtain. Smyth's view (" Dielectric Constant and Molecular Structure," 1931, p. 160), that such a link should result in an appreciable lowering* in molecular refractivity, is negatived by the observation of Allard and Wenzke (*J. Amer. Chem. Soc.*, 1934, **56**, 1693) that the molecular refractivity of acetic acid is the same in solution in benzene and in dioxan. In the course of the present work, it was found that the molecular refractivity of ethyl alcohol in solution in butyl ether was indistinguishable from the value for the pure liquid.

Evidence from cryoscopic measurements seemed possible, for formation of a hydrogen bond between an alcohol and an ether molecule will tend to reduce the complexes which the alcohol molecules would otherwise form with one another and should therefore reduce the apparent molecular weights found by this method to values nearer that of the simple alcohol molecule. The effects of different ethers in this respect are shown in Fig. 2, which

Fig. 2.




*Ethyl alcohol in*: I, *benzene*; II, *diphenyl ether*; III, *ethyl cetyl ether*; IV, *dioxan*.

presents the data obtained from cryoscopic measurements in diphenyl ether, ethyl cetyl ether, and dioxan. For comparison, the data obtained by Beckmann (*Z. physikal. Chem.*, 1888, **2**, 715) for ethyl alcohol in benzene solution are included. The rate of increase of apparent molecular weight with increasing ethyl alcohol concentration diminishes progressively through the series of solvents: benzene > diphenyl ether > ethyl cetyl ether > dioxan, the difference between diphenyl ether and dioxan being very marked. It must, however, be borne in mind that each molecule of dioxan can form links with two alcohol molecules, and moreover has such a low molecular weight that removal of dioxan as complex will be slow to show its effect. Ethyl cetyl ether has the disadvantage that, owing to its very high molecular weight, any complex formation with the solute will result in rather rapid removal of solvent and more rapid increase in apparent molecular weight of the solute.

## Experimental.

*Materials.*—For methods of purification of ethers see Part I (*loc. cit.*). The di*iso*propyl ether had been subjected to prolonged drying over sodium, and the fraction used distilled at 68·4—68·5°/764 mm. It had $d_{4^\circ}^{20^\circ}$ 0·72376, $d_{4^\circ}^{25^\circ}$ 0·81849, $\epsilon_{25^\circ}$ 3·9511. The di-*n*-butyl ether had $d_{4^\circ}^{25^\circ}$ 0·76569, $\epsilon_{25^\circ}$ 3·0866, and the diamyl ether $d_{4^\circ}^{25^\circ}$ 0·77165, $\epsilon_{25^\circ}$ 2·8220. The dioxan was

1 : 4-dioxan "pure for molecular weight determinations," m. p. 12°, $d_{4^\circ}^{25^\circ}$ 1·0272, $\epsilon_{25^\circ}$ 2·2874. The ethyl alcohol was "absolute" alcohol freshly distilled from calcium oxide, b. p. 78·2°/758 mm., $n_D^{25^\circ}$ 1·35956. The diphenyl ether had m. p. 27°. Ethyl cetyl ether was prepared by adding cetyl iodide (1 mol.) to sodium ethoxide (2 mols.) in ethyl alcohol, and warming the mixture on the water-bath for a few hours. The solid obtained on pouring the reaction mixture into excess of ice water was filtered off, recrystallised from ethyl alcohol, and finally distilled under reduced pressure to remove last traces of ethyl alcohol. The main fraction distilled at 128—130°/80 mm., and froze at 19°.

*Polarisation Measurements.*—These were made by using the apparatus described in Part I (*loc. cit.*). In the following tables the symbols have the usual significance.

| $f_2$. | $d_{4^\circ}^{25^\circ}$. | $\epsilon_{25^\circ}$. | $P_2$. | $f_2$. | $d_{4^\circ}^{25^\circ}$. | $\epsilon_{25^\circ}$. | $P_2$. |
|---|---|---|---|---|---|---|---|
| *Ethyl alcohol in isopropyl ether.* | | | | *Ethyl alcohol in dioxan.* | | | |
| 0·0000 | 0·71849 | 3·9511 | — | 0·0000 | 1·0272 | 2·2874 | — |
| 0·021581 | 0·71953 | 4·0738 | 92·6 | 0·024672 | 1·0229 | 2·4021 | 80·6 |
| 0·027171 | 0·71984 | 4·1066 | 92·6 | 0·037793 | 1·0209 | 2·4682 | 81·0 |
| 0·045242 | 0·72081 | 4·2190 | 93·2 | 0·047006 | 1·0194 | 2·5220 | 82·7 |
| 0·050011 | 0·72104 | 4·2490 | 93·2 | 0·07072 | 1·0151 | 2·6545 | 83·0 |
| 0·055746 | 0·72148 | 4·2878 | 93·2 | 0·08905 | 1·0120 | 2·7660 | 83·3 |
| 0·068176 | 0·72186 | 4·3705 | 93·4 | 0·11593 | 1·0073 | 2·9445 | 83·8 |
| 0·08093 | 0·72252 | 4·4573 | 93·4 | 0·13137 | 1·0045 | 3·0437 | 83·3 |
| 0·087129 | 0·72278 | 4·5010 | 93·0 | 0·15299 | 1·0008 | 3·2077 | 83·5 |
| 0·10565 | 0·72393 | 4·6357 | 92·5 | 0·24135 | 0·98395 | 3·9985 | 83·1 |
| 0·11609 | 0·72461 | 4·7219 | 92·68 | 0·29178 | 0·97411 | 4·5555 | 82·1 |
| | $_\infty P_2$ = 91·9. | | | | $_\infty P_2$ = 79·2. | | |

| $f_2$. | $d_{4^\circ}^{25^\circ}$. | $\epsilon_{25^\circ}$. | $P_2$. | $f_2$. | $d_{4^\circ}^{25^\circ}$. | $\epsilon_{25^\circ}$. | $P_2$. |
|---|---|---|---|---|---|---|---|
| *Ethyl alcohol in n-butyl ether.* | | | | *Ethyl alcohol in amyl ether.* | | | |
| | | | | 0·0000 | 0·77165 | 2·8220 | — |
| 0·0000 | 0·76569 | 3·0806 | — | 0·019581 | 0·77175 | 2·8989 | 104·9 |
| 0·039544 | 0·76611 | 3·2382 | 98·0 | 0·039928 | 0·77187 | 2·9475 | 100·7 |
| 0·060722 | 0·76633 | 3·3275 | 97·2 | 0·056048 | 0·77194 | 2·9982 | 99·1 |
| 0·094229 | 0·76680 | 3·4787 | 96·2 | 0·07675 | 0·77198 | 3·0689 | 98·4 |
| 0·12707 | 0·76703 | 3·6434 | 95·9 | 0·12261 | 0·77225 | 3·2353 | 97·0 |
| 0·14974 | 0·76728 | 3·7612 | 95·1 | 0·22817 | 0·77277 | 3·7132 | 95·1 |
| 0·20414 | 0·76793 | 4·0993 | 94·8 | 0·32833 | 0·77337 | 4·3804 | 94·8 |
| | $_\infty P_2$ = 99·5. | | | | $_\infty P_2$ = 112. | | |

*Cryoscopic Measurements.*—These were made with the Beckmann apparatus, the usual precautions being adopted. In diphenyl ether excessive supercooling (3—4°) takes place and a modification of the usual procedure, suggested by Dr. R. Wright of this University, has been successfully used. A fair amount of the solvent is frozen out from the solution and allowed to become warm. Until the freezing point is reached the rate of heating is very slow and the change of rate once the freezing point is passed is very marked. In practice, it is sufficient to stir at a steady rate and count the number of strokes for each successive rise in temperature of 0·01°. $\Delta t$ is the observed depression of freezing point when $w$ g. of solute are dissolved in $W$ g. of solvent.

| Solvent. | Solute. | $W$. | $w$. | $\Delta t$. | $K$. |
|---|---|---|---|---|---|
| Dioxan | Naphthalene | 25·46 | 0·3274 | 0·34° | 4·87 |
| | | | 0·4313 | 0·63 | 4·75 |
| | Dinitrobenzene | 21·27 | 0·4297 | 0·57 | 4·74 |
| | | | 0·6841 | 0·91 | 4·75 |
| Ethyl cetyl ether | Benzene | 11·07 | 0·1492 | 0·78 | 4·51 |
| | | | 0·2250 | 1·15 | 4·42 |
| | Hexane | 13·64 | 0·1013 | 0·39 | 4·52 |
| | | | 0·1800 | 0·69 | 4·50 |
| Diphenyl ether | Naphthalene | 21·09 | 0·2574 | 0·72 | 7·55 |
| | | | 0·4385 | 1·24 | 7·63 |

Average values of $K$ are: dioxan 4·78, ethyl cetyl ether 4·49, diphenyl ether 7·59. For dioxan, Oxford (*Biochem J.*, 1935, **28**, 1326) gives 4·7, Eigenberger (*J. pr. Chem.*, 1931, **130**, 75) 4·8, and Kraus and Vingee (*J. Amer. Chem. Soc.*, 1934, **56**, 511) 4·63. For diphenyl ether, Durand and Rouge (*Bull. Soc. chim.*, 1925, **37**, 697) give 7·96.

In the following table the solute in each case is ethyl alcohol.

| *w.* | *Δt.* | *M.* |
|---|---|---|
| In dioxan ($W = 21{\cdot}28$). | | |
| 0·1571 | 0·71° | 49·7 |
| 0·3082 | 1·35 | 51·3 |
| 0·5474 | 2·41 | 53·5 |
| 0·7883 | 3·22 | 55·0 |
| 1·0564 | 4·14 | 57·3 |

| *w.* | *Δt.* | *M.* |
|---|---|---|
| In ethyl cetyl ether ($W = 13{\cdot}60$). | | |
| 0·0643 | 0·37° | 57·4 |
| 0·1216 | 0·64 | 62·7 |
| 0·1655 | 0·84 | 65·0 |
| 0·2265 | 1·05 | 71·2 |
| 0·2801 | 1·24 | 74·6 |

| *w.* | *Δt.* | *M.* |
|---|---|---|
| In diphenyl ether ($W = 19{\cdot}90$). | | |
| 0·3710 | 1·87° | 75·7 |
| 0·5818 | 2·42 | 91·7 |
| 0·8808 | 2·94 | 114·6 |
| In diphenyl ether ($W = 19{\cdot}50$). | | |
| 0·3005 | 1·71 | 68·0 |
| 0·4743 | 2·28 | 81·0 |
| 0·6081 | 2·61 | 90·7 |

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## 94. *Interaction of Ketones, Carbon Monoxide, and Steam.*

By DOUGLAS V. N. HARDY.

Organic acids have been obtained from acetone and methyl ethyl ketone by high-pressure treatment with carbon monoxide and steam in presence of phosphoric acid. It is shown that the ketones condense to mesityl oxide and homomesityl oxide, respectively, which undergo hydrolytic fission into lower acids and olefins. In presence of carbon monoxide these olefins pass mainly into higher acids, but in absence of that gas they undergo polymerisation. Consideration is given to the possibility of preparing from acetone a liquid fuel of high octane number.

CERTAIN aliphatic acids are obtained when alcohols and olefins are treated under pressure with carbon monoxide and steam in presence of phosphoric acid (Hardy, J., 1934, 1335; 1936, 358, 362, 364). *iso*Butyric acid was thus obtained from the two propyl alcohols and from propylene, whereas trimethylacetic and methylethylacetic acids were formed from the butanols and from $\Delta^2$-butylene. It seemed possible that unsaturated acids of commercial importance would arise if this treatment were applied to ketones in view of their ability to react in the enolic condition. This possibility was negatived by experiment but, on the other hand, *saturated* acids were freely produced both from acetone and from methyl ethyl ketone * by a reaction of somewhat novel character. The experiments were carried out under a pressure of 200 atm., and a mixture of ketone and water vapours was led with carbon monoxide through liquid phosphoric acid at 200—210°. Acidity of the product was governed most markedly by reaction temperature, as is shown by the following data, which refer to methyl ethyl ketone:

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Reaction temp. | 146° | 165° | 169° | 174° | 179° | 185° | 191° | 195° | 200° | 205° | 210° |
| Acidity of product (N) | 0·66 | 1·32 | 1·90 | 2·10 | 2·27 | 2·5 | 2·7 | 2·8 | 3·0 | 3·0 | 2·5 |

Acetone gave rise to a mixture of acetic and trimethylacetic acids in the approximate molecular ratio of 2 : 1. A small proportion of more complex acids was also present, together with a mixture of unsaturated neutral substances consisting chiefly of hydrocarbons. These observations find a simple and adequate explanation on the assumption that reaction proceeds by way of mesityl oxide, which undergoes hydrolytic fission into *iso*butylene and acetic acid:

$$2COMe_2 \longrightarrow CMe_2{:}CH\overset{H|OH}{|}CO{\cdot}Me \longrightarrow CMe_2{:}CH_2 + Me{\cdot}CO_2H$$

Part of the *iso*butylene undergoes polymerisation into higher olefins, and the remainder reacts with carbon monoxide and steam in known fashion (Hardy, J., 1936, **358**, 362):

$$CMe_2{:}CH_2 + H_2O + CO \longrightarrow CMe_3{\cdot}CO_2H$$

* The essential features of this work were completed (see British Patent Application No. 18330/2.7.1936) without knowledge of U.S.P. 2,037,684 (A. T. Larson, Assr. to E. I. Du Pont de Nemours & Co., granted, 14.4.36; date of application, 25.5.33. See *British Chemical Abstracts*, *B*, 417, 1937) which claims the production of acetic and trimethylacetic acids from acetone, and of unspecified acids from other ketones including methyl ethyl ketone.

This hydrolytic fission of mesityl oxide finds a parallel in the formation of acetic and α-hydroxy*iso*butyric acids by permanganate oxidation of mesityl oxide (Pinner, *Ber.*, 1882, **15**, 591), and recalls a synthesis of the latter from *iso*butylene and acetyl chloride or acetic anhydride in presence of aluminium and zinc halides (Kondakow, *J. Russ. Phys. Chem. Soc.*, 1894, **26**, 12, 232; Krapiwin, *Chem. Zentr.*, 1910, I, 1336). Confirmation of the foregoing mechanism has been obtained by treating mesityl oxide with carbon monoxide and steam in presence of phosphoric acid, acetic and trimethylacetic acids being readily obtained. Moreover, if hydrogen or nitrogen be employed in place of carbon monoxide, acetone yields acetic acid together with an increased amount of neutral unsaturated oil, this reaction being independent of pressure. In absence of carbon monoxide, therefore, formation of trimethylacetic acid is impossible, and the only course of reaction left open to the *iso*butylene is polymerisation. Attempts to isolate *iso*butylene itself as a product of reaction have been unsuccessful, so it would appear that the conditions necessary for bringing about hydrolytic fission are too severe to allow the survival of the olefin.

When methyl ethyl ketone was treated with carbon monoxide, acids and unsaturated neutral oils were again produced. The acid mixture was, however, more complex, and the following constituents have been identified: acetic, propionic, αα-dimethylbutyric ($CMe_2Et{\cdot}CO_2H$), αα-dimethylvaleric ($CMe_2Pr{\cdot}CO_2H$), and α-methyl-α-ethylbutyric ($CMeEt_2{\cdot}CO_2H$). Acetic acid and the two heptoic acids constituted the bulk of the mixture and can only have been produced by hydrolytic fission of γδ-dimethyl-$\Delta^{\gamma}$-hexen-β-one:

$$\begin{array}{c} \mathrm{H{\vdots}OH} \\ \mathrm{2COMeEt \longrightarrow CMeEt{:}CMe{-}{\vdots}{-}COMe \longrightarrow CMeEt{:}CHMe + Me{\cdot}CO_2H} \\ \mathrm{CMeEt{:}CHMe + CO + H_2O \longrightarrow CMeEt_2{\cdot}CO_2H} \end{array}$$

The formation of αα-dimethylvaleric acid definitely involves a molecular transformation which is most likely to occur by isomerisation of γ- into β-methyl-$\Delta^{\beta}$-pentene:

$$\mathrm{CMeEt{:}CHMe \longrightarrow CHEt{:}CMe_2 \xrightarrow{CO + H_2O} CH_2Et{\cdot}CMe_2{\cdot}CO_2H}$$

Such a rearrangement involving the exchange of an alkyl group for hydrogen across an unsaturated link has already been encountered in this series of experiments (J., 1936, 362, 364, and unpublished observations) and it would now appear that it is of the Wagner–Meerwein type.* The two remaining acids, propionic and αα-dimethylbutyric, must on the other hand have been formed from γ-methyl-$\Delta^{\gamma}$-hepten-ε-one:

$$\begin{array}{c} \mathrm{H{\vdots}OH} \\ \mathrm{2COMeEt \longrightarrow CMeEt{:}CH{-}{\vdots}{-}CO{\cdot}Et \longrightarrow CMeEt{:}CH_2 + Et{\cdot}CO_2H} \\ \mathrm{CMeEt{:}CH_2 + CO + H_2O \longrightarrow CMe_2Et{\cdot}CO_2H} \end{array}$$

so it is fairly evident that, in presence of phosphoric acid under the experimental conditions, methyl ethyl ketone condenses with itself to give a mixture of dimethylhexenone and methylheptenone in which the former predominates. This conclusion is in agreement with the observations of Abbott, Kon, and Satchell (J., 1928, 2514), who found that acid catalysts favour the formation of dimethylhexenones whereas alkaline agents lead to methylheptenones (cf. Powell and Secoy, *J. Amer. Chem. Soc.*, 1931, **53**, 765; Grignard and Cologne, *Compt. rend.*, 1930, **190**, 1349).

Attempts to apply this process to other ketones have so far met with little success. No acid could be obtained from *cyclo*hexanone, whereas diethyl ketone gave in very small yield a mixture of propionic acid and an unidentified heptanoic acid instead of the anticipated octanoic acid. Evidently the olefin derived by hydrolytic fission of δ-methyl-ε-ethyl-$\Delta^{\delta}$-hepten-γ-one had lost a methyl group in exchange for a hydrogen atom:

$$\begin{array}{c} \mathrm{H{\vdots}OH} \\ \mathrm{2COEt_2 \longrightarrow CEt_2 = CMe{-}{\vdots}{-}COEt \longrightarrow CEt_2{:}CHMe + Et{\cdot}CO_2H} \end{array}$$

probably by interchange with another molecule:

$$\mathrm{2CEt_2{:}CHMe \longrightarrow CEt_2{:}CH_2 + CEt_2{:}CMe_2}$$

* Grateful acknowledgment is made to Professor J. Kenner, who advanced this suggestion at a lecture given by the author in Manchester on October 2nd, 1936.

*but the amount of material was inadequate for a full investigation of this matter. The existence of such an olefinic interchange has been demonstrated in the case of the amylenes (unpublished observation) by the isolation of acids with one more and one less carbon atom than that which would be produced by normal reaction with carbon monoxide and steam.*

The production of trimethylacetic acid from acetone demonstrated the transient existence of *iso*butylene and directed attention to the possibility of producing a fuel of high octane number from acetone by treatment with steam in presence of phosphoric acid and an inert gas such as nitrogen or hydrogen. Hydrogenation of the neutral unsaturated material so obtained yielded a spirit fraction (b. p. <200°) which had an octane number of 81 and was miscible with ordinary motor spirit. This relatively low octane number is a little surprising in view of the fact that the material has its origin in *iso*butylene, but the conditions of polymerisation are severe and may lead to hydrocarbons with poor anti-detonation characteristics. This suggestion has already been advanced by Ipatieff and Komarewsky (*Ind. Eng. Chem.*, 1937, **29**, 958) to account for the low octane numbers (83 and 84) of octane fractions (b. p. 100—125°) obtained by simultaneous polymerisation and hydrogenation of *iso*butylene in presence of a phosphoric acid–iron–nickel oxide catalyst at 250° and 300°.

## EXPERIMENTAL.

The apparatus and experimental technique were substantially as described previously (J., 1934, 1339), and 400 c.c. of 87% phosphoric acid were employed uniformly as catalyst. Except where otherwise stated, the pressure was 200 atm. and the rate of circulation was 40 l. of compressed gas per hour.

The products were worked up according to the following procedure, designed to permit an almost complete recovery of anhydrous acids. After addition of slightly more than the theoretical quantity of potassium hydroxide solution (50%), the products were distilled to remove unchanged ketone. Residual oil was separted from the aqueous solution of salts, and the latter was evaporated to dryness and dried in a vacuum at 200°. A considerable excess of anhydrous phosphoric acid was then added to the dry salts, and the liberated acids were recovered by distillation (oil-bath) first under ordinary and then under reduced pressure. The acid distillate still contained a small amount of water which was removed by azeotropic distillation with benzene, and the anhydrous acids were distilled fractionally through a 4′ electrically-heated Dufton column.

*Acetone and Carbon Monoxide.*—A mixture of acetone (1450 g.) and water (362 g.) was injected into the vaporiser at the rate of 280 c.c. per hour, and at a reaction temperature of 200—205° gave a product (1720 g.; C, 49·4; acidic H, 0·47%) from which unchanged acetone (514 g.) and unsaturated oil (188 g.; C, 85·1; H, 11·2%) were isolated. From these data the carbon balance (in g.) could be calculated:

| | | |
|---|---|---|
| Carbon introduced as acetone | 900 | — |
| ,, ,, CO (*estimated*) | 32 | — |
| Carbon accounted for as recovered acetone | — | 319 |
| ,, ,, acids | — | 371 |
| ,, ,, neutral oils | — | 160 |
| ,, ,, substances scrubbed from the waste gases by conc. $H_2SO_4$ | — | 21·5 |
| Loss | — | 60·5 |
| Total | 932 | 932 |

The acids (550 g.) were distilled as follows:

| B. p. | 116—125° | 125—155° | 155—161° | 161—164° | 164—166° | 166—170° | 170—185° | Residue |
|---|---|---|---|---|---|---|---|---|
| Weight (g.) | 262·5 | 9·4 | 1·3 | 33·3 | 196 | 13·7 | 6·8 | 27 |

The fraction of b. p. 116—125° was acetic acid and gave *p*-phenylphenacyl acetate, m. p. 109—109·5° and mixed m. p. 110°. The fraction, b. p. 164—166°, which crystallised on cooling, was shown to be trimethylacetic acid by conversion into its anilide, m. p. and mixed m. p. 132—133°.

*Mesityl Oxide and Carbon Monoxide.*—The vaporiser was initially filled with water, heated to 110°, and mesityl oxide was injected at the rate of 220 c.c. per hour. At a reaction temperature of 200° the product was homogeneous and contained 0·54% of acidic hydrogen. After neutralisation, 1122 g. of product gave a distillate, the upper layer of which was re-distilled:

| B. p. | <80° (A) | 80—100° (B) | 100—140° (C) | Residue (D) |
|---|---|---|---|---|
| Weight (g.) | 13 | 33 | 236 | 135 |

A, B, and C consisted respectively of acetone, the constant-boiling mixture of mesityl oxide and water (b. p., *ca.* 92·2°), and mesityl oxide (Found : C, 73·4; H, 10·1. Calc. for $C_6H_{10}O$ : C, 73·5; H, 10·2%). The residue from the first distillation consisted of an upper layer of dark oil (58·5 g.; C, 80·7; H, 11·1%) and an aqueous solution of salts, from which 318 g. of acids were isolated :

| | | | | | | |
|---|---|---|---|---|---|---|
| B. p. .................. | 117—125° | 125—141° | 141—160° | 160—163° | 163—165° | Residue |
| Weight (g.) ........... | 193 | 2·5 | 4 | 19 | 73 | 23·5 |

The fraction of b. p. 117—125° was acetic acid (*p*-phenylphenacyl acetate, m. p. and mixed m. p., 109·5—110°), and that of b. p. 163—165° was trimethylacetic acid, which crystallised on cooling and was identified by conversion into anilide, m. p. 130—130·5° and mixed m. p. 130·5—131°.

*Methyl Ethyl Ketone and Carbon Monoxide.*—In 6 hours a mixture of methyl ethyl ketone (1042 g.) and water (116 g.) was vaporised and led with carbon monoxide through the catalyst at 200°. The product (1253 g.) consisted mainly of an upper layer (1070 g.; C, 56·5; acidic H, 0·33%), together with a small lower layer (183 g.; C, 15·1%). After small samples had been taken for analysis, the product (1065 g. of upper, and 181·7 g. of lower layer) was made alkaline and was distilled up to 85° to remove the binary mixture of methyl ethyl ketone and water (597 g.; C, 60·15%). Further distillation, with addition of water when necessary, gave a steam-volatile oil (58·3 g.; C, 77·6; H, 11·6%), and a residual non-volatile oil (38·3 g.; C, 80·5; H, 11·4%) was extracted with petroleum (b. p. 40—60°) from the aqueous solution of salts. These data lead to the following carbon balance (in g.) :

| | | |
|---|---|---|
| Carbon introduced as COMeEt ............ | 695 | — |
| ,, ,, CO (estimated) ............ | 20 | — |
| Carbon accounted for as recovered COMeEt ............ | — | 304 |
| ,, ,, oil (steam-volatile) ............ | — | 45·4 |
| ,, ,, oil (non-volatile) ............ | — | 31 |
| ,, ,, acids ............ | — | 192·6 |
| ,, ,, products scrubbed from exit gases by conc. $H_2SO_4$ ............ | — | 45 |
| Loss ............ | — | 37 |
| Total ............ | 715 | 715 |

From the dried potassium salts, 315 g. of anhydrous acids were isolated, and were separated into the following fractions :

| | | | | | | |
|---|---|---|---|---|---|---|
| B. p. .................. | <115° | 115—123° | 123—136° | 136—144° | 144—175° | 175—180° |
| Wt. (g.) .............. | 6·2 | 81·5 | 7·9 | 20·9 | 22·8 | 2·4 |
| B. p. .................. | 180—190° | 190—195° | 195—202° | 202—210° | Residue | |
| Wt. (g.) .............. | 39·4 | 13·0 | 34·8 | 46·4 | 28·1 | |

The fraction of b. p. 115—123° was shown to be acetic acid by conversion into *p*-phenylphenacyl acetate, m. p. and mixed m. p. 109°, whereas that of b. p. 136—144° was propionic acid (Found : equiv., 75. Calc. : equiv., 74). It was identified by means of its *p*-phenylphenacyl ester, m. p. 96° and mixed m. p. with an authentic specimen (m. p. 100°) 98—99°. The fraction of b. p. 182—190° (Found : equiv., 114. Calc. for $C_6H_{12}O_2$ : equiv., 116) contained αα-dimethylbutyric acid and was converted into amide (m. p. 101°; mixed m. p. 102—103° with authentic material of m. p. 102—103°), anilide (m. p. 89°; mixed m. p. 90·5—91°), and *p*-phenylphenacyl ester (m. p. 82—84°). Wrede and Rothhaus (*Ber.*, 1934, **67**, 739) give 86·5° as the m. p. of *p*-phenylphenacyl αα-dimethylbutyrate. The material, b. p. 202—210°, contained two difficultly-separable heptoic acids (Found : equiv., 131. Calc. : equiv., 130), the amides of which differed markedly, one crystallising in plates and the other in needles. By careful fractional distillation of a greater quantity, the material was divided into fractions as follows :

| | | | | | | |
|---|---|---|---|---|---|---|
| B. p. .............. | 200—202° | 202—205° | 205—207° | 207—208·4° | 208·4—208·6° | Residue |
| Wt. (g.) .......... | 2·5 | 28·9 | 60·7 | 58·8 | 6·9 | 8·0 |

The acid of b. p. 202—205° gave an amide which crystallised from petroleum (b. p. 40—60°) in plates, m. p. 93—94°, and did not depress the m. p. of authentic αα-dimethylvaleramide (m. p. 94·5°). Fraction b. p. 208·4—208·6° was shown to be α-methyl-α-ethylbutyric acid by preparing the amide [needles, m. p. 74—75°; mixed m. p. with authentic material (m. p. 75·5—76°) 74—75·5°] and anilide [needles from petroleum (b. p. 60—80°), m. p. 84—85°; mixed m. p. 85—86° with an authentic specimen of m. p. 87—87·5°].

*Diethyl Ketone and Carbon Monoxide.*—In this experiment the vaporiser was filled with water and heated to 100°. Diethyl ketone was then pumped in at the rate of 100 c.c. per hour. The resulting vapours were led with carbon monoxide through the catalyst whose temperature was

gradually raised from 190° to 290°. At intervals the product was withdrawn, and titrated with standard alkali:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Reaction temp. ...... | 189° | 199° | 204° | 212° | 225° | 233° | 241° | 250° | 260° | 276° |
| Acidity (N) ........... | 0·26 | 0·39 | 0·42 | 0·51 | 0·65 | 0·67 | 0·53 | 0·65 | 0·51 | 0·37 |

The acids from the combined material were distilled as follows:

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| B. p. ...... | <136° | 136—143° | 143—160° | 160—215° | 215—220° | 220—225° | Residue |
| Wt. (g.) ... | 0·5 | 6·3 | 5·3 | 1·0 | 4·6 | 2·0 | 3·4 |

The acid of b. p. 136—143° gave an anilide, m. p. and mixed m. p. with authentic propionanilide, 104°. The acid of b. p. 215—220° (Found: equiv., 133, 134. Calc. for $C_6H_{13}{\cdot}CO_2H$: equiv., 130) gave an anilide which crystallised from light petroleum (b. p. 40—60°) in colourless needles, m. p. 92—94°, and after recrystallisation the first fraction melted sharply at 110°. It also gave a very soluble anilide, obtained as colourless needles, m. p. 86—89°, from petroleum (b. p. <40°).

*Acetone and Nitrogen.*—A mixture of acetone and water (4 : 1 by wt.) was injected into the vaporiser at 95°, and the vapours were led with nitrogen under 120 atm. through the catalyst at 200—205°. The product consisted of an upper yellow-brown oil and a lower acidic layer, and the ratio of upper to lower layer varied from 1 : 5 to 1 : 3 by volume. The total product (1262 g.) contained 319 g. of upper layer (C, 85·5, 85·7; H, 12·4, 12·3%) and 943 g. of lower layer (C, 40·4, 40·2; H, 10·1, 10·4; acidic hydrogen, 0·33%, *i.e.*, acetic acid, 19·8%). The lower layer (909 g.) was neutralised with potassium hydroxide and distilled up to 80°, unchanged acetone (477 g.) being recovered. It was substantially free from hydrocarbons since, on dilution, no upper layer separated. The residue from the distillation contained a very small upper layer which was volatile in steam and appreciably soluble in water (mesityl oxide ?). From the salts, acetic acid (70 g. of b. p. 117—120°) was isolated and identified by conversion into *p*-phenylphenacyl acetate, m. p. 107—108°, mixed m. p. 107—108·5°. The oily upper layer (291 g.) was dried and neutralised over potassium hydroxide and then distilled to 75° to remove acetone (35 g.). The residue was distilled:

| | | | | | | |
|---|---|---|---|---|---|---|
| B. p. .................... | —100° | 100—150° | 150—200° | 200—250° | 250—315° | Residue |
| Wt. (g.) .................. | negligible | 8·8 | 32 | 86·1 | 87·6 | 16 |

The material, b. p. 100—315°, was catalytically hydrogenated in presence of nickel–kieselguhr at 200° and at 100 atm. (initial). Absorption of hydrogen was slow. The product was separated by distillation into fractions, the properties of which were as follows:

| Fraction. | %. | $d^{24°}$. | Composition. C, %. | Composition. H, %. | Fraction. | %. | $d^{24°}$. | Composition. C, %. | Composition. H, %. |
|---|---|---|---|---|---|---|---|---|---|
| <100° | 3·5 | — | — | — | 200—250 | 37·9 | 0·839 | 85·3 | 12·9 |
| 100—150 | 3·7 | 0·737 | 81·8 | 14·5 | 250—300 | 38·0 | 0·893 | 86·3 | 12·2 |
| 150—200 | 8·3 | 0·797 | 84·5 | 13·5 | Residue | 8·6 | — | — | — |

Similar products were obtained by working at 30 atm. and at 10 atm.

*Acetone and Hydrogen.*—The vapour from 80% acetone was led with hydrogen under 30 atm. through the catalyst at 200—220°. Starting with 5228 g. of acetone, 2180 g. of which were recovered and resubmitted to the catalyst, 1650 g. of oil were obtained. The portion of the oil boiling below 185°/100 mm. was exhaustively treated with hydrogen under 120 atm. (initial) in presence of nickel–keiselguhr catalyst, and the resulting material was distilled up to 200°. The distillate had a sweet and pleasant odour unlike that of petrol. It had $d^{20°}$ 0·775, and octane number 81.

*Authentic Specimens.*—αα-Dimethylbutyric, αα-dimethylvaleric and α-methyl-α-ethylbutyric acids were prepared by hydrolysing with 25% sulphuric acid the amides formed from the appropriate ωωω-substituted acetophenones by treatment with sodamide (Haller and Bauer, *Compt. rend.*, **1909**, **148**, 70). The substituted acetophenones were prepared by alkylating *iso*- or *n*-butyrophenone (*idem, ibid.*, p. 129). Two of the anilides had not hitherto been prepared. *αα-Dimethylvaleranilide* (Found: N, 6·83. $C_{13}H_{19}ON$ requires N, 6·83%) and *α-methyl-α-ethylbutyranilide* (Found: N, 6·83%) crystallised in needles, m. p. 73·5° and 87—87·5° respectively.

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# 95. *The Action of Acid Chlorides on Anilides.*

By C. A. Friedmann and O. G. Backeberg.

It has been found that substituted amidines are usually formed when anilides react with acid chlorides; the yield of amidine from formanilide is almost quantitative, whereas the amounts formed from other anilides are relatively small. Hübner and collaborators observed the formation of basic by-products in the reaction, but failed to identify the bases. Paal and Otten reported that the reaction yielded a small quantity of by-product which they regarded as hydrazobenzene; this, too, has been found to be a substituted amidine. A mechanism for the formation of amidines in the reaction is proposed.

The descriptions of this reaction, which was investigated by Hübner and Frerichs (*Ber.*, 1877, **10**, 1720), Hübner, Frerichs, and Meyer (*ibid.*, p. 2165), Paal and Otten (*Ber.*, 1890, **23**, 2587), Pictet (*ibid.*, p. 3011), and Kay (*Ber.*, 1893, **26**, 2853), under conditions varying from the comparatively mild treatment of Hübner to the more vigorous conditions employed by Kay, require amplification and correction in some respects.

Hübner and his collaborators (*locc. cit.*) reported that acetanilide and benzanilide reacted with succinyl chloride or other acid chlorides to form bases which they described, without reporting any analyses, as $C_{29}H_{28}N_4$, m. p. 132—134°, and $C_{42}H_{36}N_4$, m. p. 217°, respectively. These bases have been found to be diphenylacetamidine, $C_{14}H_{14}N_2$, m. p. 132°, and diphenylbenzamidine, $C_{19}H_{16}N_2$, m. p. 144°; the close correspondence between the analytical values required by the two sets of molecular formulæ leaves little room for doubt that these were the substances they described. A product having m. p. 217° could not be obtained from succinyl chloride and benzanilide.

Paal and Otten (*loc. cit.*), in attempting to prepare diacylanilides, treated the sodium derivatives of anilides with acid chlorides, and reported that in the case of sodium form- or acet-anilide, in addition to the anilide produced by an exchange reaction, a small quantity of a compound was formed which they regarded as hydrazobenzene. It has been found that this substance is diphenylformamidine when derived from formanilide, and diphenylacetamidine when derived from acetanilide.

Pictet (*loc. cit.*) also attempted to prepare diacylanilides, using the anilides themselves instead of their sodium derivatives; he reported that between 100° and 150° an exchange reaction occurred almost quantitatively, the reaction being limited in that it only took place if the acid chloride used were of higher molecular weight than that derived from the acid radical of the anilide. This has been confirmed, and, in addition, it has been found that some substituted amidine is always formed. The quantity of this amidine varies from traces in most cases to appreciable quantities when acetanilide is used; with formanilide the yield of diphenylformamidine is almost quantitative, and it is surprising that Pictet, who studied the reaction in detail, failed to make this observation.

Kay's observation that diacylanilides are formed under the more vigorous reaction conditions used by him—200° for 3—4 hours—has been confirmed. It was also found that under these conditions reversal of Pictet's exchange reaction takes place to some extent, and that traces of basic substances, usually insufficient for identification, are also formed.

The following scheme is proposed for the mechanism of amidine formation (compare Stephen and Bleloch, J., 1931, 886; Backeberg, *ibid.*, p. 2814):

$$\text{R·CO·NHPh} + \text{R·C(OH)}\!:\!\text{NPh} \xrightarrow{-H_2O} \text{R·CO·NPh·CR}\!:\!\text{NPh} \xrightarrow{H_2O} \text{NHPh·CR}\!:\!\text{NPh} + \text{R·CO}_2\text{H}$$

The condensing agent is probably hydrogen chloride, for it is significant that in the case of formanilide, in which hydrogen chloride is liberated in large quantity, the yield of amidine is very much greater than in the other cases (compare Wallach, *Ber.*, 1882, **15**, 208).

## Experimental.

The substituted amidine was isolated by acidifying the end-product of the reaction with cold dilute hydrochloric acid and precipitating the base from the filtered solution with ammonia. All substances were identified by mixed m. p. determinations with authentic specimens, and the bases were further identified by means of their picrates. All refluxing apparatus was fitted with a calcium chloride tube to exclude atmospheric moisture.

*Reactions of Formanilide.*—Formanilide was obtained free from diphenylformamidine by distillation nnder diminished pressure. 8 C.c. of acetyl chloride were added to 11 g. of formanilide and heated under reflux to 100° during 1 hour; at about 45° a vigorous reaction set in, carbon monoxide and hydrogen chloride being evolved. The product, m. p. 259°, consisted of almost pure diphenylformamidine hydrochloride; extraction with hot water gave 0·5 g. of acetanilide. During the extraction much of the amidine was decomposed by hydrolysis; when the solution was made alkaline, 6 g. of diphenylformamidine were obtained, m. p. 139° after crystallisation from benzene or dilute alcohol. This amidine is considerably less stable than either diphenylacet- or benz-amidine; a specimen kept in a corked tube underwent considerable decomposition after several months. The hydrochloride is very readily soluble in cold water, but only sparingly so in dilute hydrochloric acid (2·84 g. in 100 c.c. of 2N-hydrochloric acid at 18°).

Similar results were obtained under the same conditions by the reaction between formanilide and propionyl or benzoyl chloride, except that the yield of amidine was slightly less, and of the corresponding anilide somewhat greater.

*Reactions of Acetanilide.*—(i) *With acetyl chloride.* 20 G. of acetanilide were refluxed with 100 c.c. of acetyl chloride for 7 hours: the excess of acetyl chloride was then removed under diminished pressure. From the residue, which was mainly unchanged acetanilide, 2 g. of diphenylacetamidine, m. p. 132°, were extracted. Similar resnlts were obtained when equivalent quantities of the reagents and a temperature of 120° was used according to Pictet (*loc. cit.*) or if the temperature was raised to 180° according to Kay (*loc. cit.*). The yield of amidine was, however, somewhat smaller.

(ii) *With propionyl chloride.* 10 G. of acetanilide and 7 c.c. of propionyl chloride were refluxed for 1 honr. From the oily product, which soon solidified on cooling, 0·2 g. of diphenylacetamidine, m. p. 132°, was obtained. The remainder of the product consisted of propionanilide.

(iii) *With succinyl chloride.* 2·4 G. of acetanilide, dissolved in 15 c.c. of chloroform, were refluxed for 7 hours with 2 c.c. of succinyl chloride. From the product, after removal of chloroform and unchanged succinyl chloride under diminished pressure, 0·05 g. of diphenylacetamidine, m. p. 132°, was obtained. The remainder of the product consisted of unchanged acetanilide.

(iv) *With benzoyl chloride.* 10 G. of acetanilide and 8 c.c. of benzoyl chloride were heated under reflux at 170° for 1 hour; the temperature was then raised to 300° for a few minutes. The product consisted almost entirely of benzanilide, and extraction with dilute hydrochloric acid gave only a small trace of basic material insufficient for identification.

*Reactions of Propionanilide.*—Treatment with acetyl chloride, propionyl chloride or benzoyl chloride by the methods mentioned gave only minute traces of basic products insufficient for identification.

*Reactions of Benzanilide.*—(i) *With acetyl chloride.* (a) 20 G. of benzanilide were refluxed with 100 c.c. of acetyl chloride for 20 hours. After removal of the excess of acetyl chloride, the residue, which was mainly unchanged benzanilide, gave 0·2 g. of diphenylbenzamidine, m. p. 144°. (b) 10 G. of benzanilide were heated under reflux with 10 c.c. of acetyl chloride at 180° for 1 hour. The product had a pronounced odour of benzoyl chloride, indicating that the reverse of Pictet's exchange reaction had taken place to some extent. This was confirmed by treatment with cold dilute aqueous caustic soda and acidification of the filtered solution, 0·1 g. of benzoic acid being obtained. The product consisted mainly of unchanged benzanilide; acid extraction gave only a trace of basic substance insnfficient for identification, and extraction with hot water gave 0·5 g. of acetylbenzanilide, m. p. 78°.

(ii) *With propionyl chloride.* 10 G. of benzanilide were heated under reflux with 8 c.c. of propionyl chloride at 200° for 1 hour. The product had a pronounced odour of benzoyl chloride. It consisted mainly of nnchanged benzanilide and, when treated as above, gave 0·1 g. of benzoic acid, 0·5 g. of propanilide, and a trace of basic substance insufficient for identification.

(iii) *With succinyl chloride.* To obtain a basic product in identifiable quantity, the reaction described by Hübner (*loc. cit.*) was carried ont in a sealed tube. 2 C.c. of succinyl chloride, 2·2 g. of benzanilide, and 10 c.c. of chloroform were heated at 100° for 8 hours. After removal of the chloroform and unchanged succinyl chloride under diminished pressure, the residue, in which the odour of benzoyl chloride was detected, consisted mainly of unchanged benzanilide. It yielded 0·05 g. of diphenylbenzamidine, m. p. 144°.

The authors thank Prof. H. Stephen for his interest in the work.

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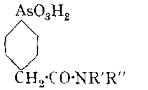
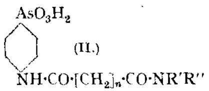
# 96. *Amides of* p-*Arsonophenylacetic Acid.*

By E. Walton.

A series of amides (I) has been prepared from *p*-arsonophenylacetic acid for comparison with compounds of type (II). These amides are all well-defined, crystalline compounds, and their sodium salts show fair activity against experimental sleeping sickness.

A series of compounds of type (I) has been prepared for comparison with similar derivatives (II) of *p*-arsanilic acid, which have been described from time to time in this Journal. These amides were prepared from *p*-arsonophenylacetic acid (Robertson and

(I.) 

 (II.)

Stieglitz, *J. Amer. Chem. Soc.*, 1921, **43**, 180) by treating its *methyl* ester with various amines in either aqueous or alcoholic solution. Their sodium salts have been tested for trypanocidal activity under the direction of Professor Warrington Yorke, F.R.S., with results as follows:

| Sodium salts. | M.L.D. | M.C.D. | Sodium salts. | M.L.D. | M.C.D. |
|---|---|---|---|---|---|
| Methyl ester | 4 | Some action | Ethylamide | 16 | 8 |
| Amide | 64 | 8—16 | *n*-Propylamide | 32 | 32 |
| Methylamide | 64 | 16 | Piperidide | 2 | No action |
| Dimethylamide | 16 | 16 | Anilide | 8 | Some action |

M.L.D. = minimum lethal dose, M.C.D. = minimum curative dose (both in mg. per 20 g. of mouse).

It will be seen that trypanocidal activity is again maintained throughout the series. In fact, from these results and from a survey of the literature, it appears that an amide group in the *p*-position of the unsubstituted phenylarsonic acid nucleus nearly always maintains or confers activity (compare *Chem. and Ind.*, 1937, **56**, 1116).

## Experimental.

*Methyl* p-*Arsonophenylacetate.*—Crude *p*-arsonophenylacetic acid (18 g.), prepared from *p*-aminophenylacetic acid according to the method of Robertson and Stieglitz (*loc. cit.*), was dissolved in methyl alcohol, and the solution slowly saturated with hydrogen chloride. It was then refluxed for 1 hour, and the residue, after removal of methyl alcohol, treated with water. The resulting *methyl* ester (11 g.) crystallised from 50% water–ethyl alcohol in long colourless needles, very soluble in hot water and alcohol (Found: As, 27·5; O·$CH_3$, 10·9. $C_9H_{11}O_5As$ requires As, 27·4; O·$CH_3$, 11·3%). The *sodium* salt crystallised from dilute alcohol in leaflets, $p_H$ 8·0 (Found: As, 24·3. $C_9H_{10}O_5AsNa,H_2O$ requires As, 23·9%).

*Phenylacetamide*-p-*arsonic Acid.*—The methyl ester (6 g.) and excess of concentrated aqueous ammonia were heated at 100° in a sealed tube for 6 hours. The resulting crimson solution gave crystals of *ammonium phenylacetamide*-p-*arsonate*, which crystallised from alcohol–water in parallelepipeds (2 g.), $p_H$ 5·0, and from concentrated aqueous solution in silky needles (Found: N, 10·1. $C_8H_{13}O_4N_2As$ requires N, 10·15%). The free *acid* crystallised from water in prisms, insoluble in alcohol (Found: N, 5·5. $C_8H_{10}O_4NAs$ requires N, 5·4%).

*Phenylacetomethylamide*-p-*arsonic Acid.*—The methyl ester (3 g.) and excess of 25% aqueous methylamine were heated under pressure at 100°, until the crimson colour that developed faded to yellow (about 5 hours); the syrup was then evaporated and acidified. The resulting *methylamide* (2 g.) crystallised from water in pale yellow, hexagonal prisms, soluble in hot alcohol (Found: N, 4·9. $C_9H_{12}O_4NAs$ requires N, 5·1%). The *sodium* salt, $p_H$ 7·0, prepared by evaporation, was somewhat deliquescent (Found: N, 4·45. $C_9H_{11}O_4NAsNa,H_2O$ requires N, 4·5%).

*Phenylacetodimethylamide*-p-*arsonic Acid.*—This cannot be prepared under aqueous conditions. The methyl ester (8 g.) and 50% alcoholic dimethylamine (30 c.c.) were heated at 100° in a sealed tube for 5 hours. The dimethylamine was completely removed, and the

residue carefully acidified and cooled in a freezing mixture. Owing to excessive solubility in water, the resulting fawn-coloured precipitate (7 g.) was crystallised from alcohol by slow addition of ether. The *dimethylamide* now crystallised from water plus a trace of hydrochloric acid in large rhombic leaflets, very soluble in alcohol (Found: N, 4·9. $C_{10}H_{14}O_4NAs$ requires N, 4·9%). Its *sodium* salt, $p_H$ 7·0, was white and indefinitely crystalline (Found: N, 4·6. $C_{10}H_{13}O_4NAsNa$ requires N, 4·5%).

*Phenylacetoethylamide*-p-*arsonic acid* was prepared as above, 33% alcoholic ethylamine being used. It was purified by dissolution in alcohol and addition of ether until a brown flocculent precipitate appeared. This was removed, and the filtrate treated with more ether until the *ethylamide* began to separate in micro-crystals. The ethylamide crystallised from water plus a trace of hydrochloric acid in long prisms (Found: N, 4·7. $C_{10}H_{14}O_4NAs$ requires N, 4·9%). Its *sodium* salt, $p_H$ 7·0, was prepared in alcohol (Found: N, 4·4. $C_{10}H_{13}O_4NAsNa$ requires N, 4·5%).

*Phenylaceto*-n-*propylamide*-p-*arsonic Acid*.—The methyl ester (4·8 g.) and 50% alcoholic *n*-propylamine were heated under pressure until the crimson colour had disappeared. The propylamine was completely removed by repeated evaporation and addition of alcohol. As the residue failed to give a solid on acidification, it was dissolved in alcohol (about 30 c.c.), to which ether (about 30 c.c.) was added to precipitate impurities. The filtrate was treated with more ether until milky, and cooled to 0°; the n-*propylamine* salt of *phenylaceto*-n-*propylamide*-p-*arsonic acid* (3·8 g.) then separated in micro-needles (Found: N, 8·1. $C_{14}H_{25}O_4N_2As$ requires N, 7·8%). The free *propylamide* crystallised from water plus a trace of hydrochloric acid in needles, soluble in alcohol (Found: N, 4·8. $C_{11}H_{16}O_4NAs$ requires N, 4·7%). Its *sodium* salt, $p_H$ 7·0, crystallised from alcohol–water in rhombic plates (Found: N, 4·5. $C_{11}H_{15}O_4NAsNa$ requires N, 4·3%).

*Phenylacetopiperidide*-p-*arsonic Acid*.—The methyl ester (7 g.) and piperidine (25 c.c.) were refluxed together for about 3 hours. The excess of piperidine was completely removed, and the residue acidified. The *piperidide* (4·5 g.), thus obtained, crystallised from water in cream-coloured hexagonal prisms, soluble in warm alcohol (Found: N, 4·3. $C_{13}H_{18}O_4NAs$ requires N, 4·3%). The *sodium* salt, $p_H$ 6·5, was prepared by evaporating its alcoholic solution (Found: N, 4·2. $C_{13}H_{17}O_4NAsNa$ requires N, 4·0%).

*Phenylacetanilide*-p-*arsonic Acid*.—*p*-Arsonophenylacetic acid (5 g.) was heated in an open beaker with excess of aniline (15 c.c.). The mixture first tended to solidify, but, on further heating, liquefied and boiled. As soon as the water had been removed, the mixture was cooled and acidified. The resulting *anilide*, after purification through sodium carbonate solution, crystallised from water, in which it was only slightly soluble, in needles, soluble in hot alcohol (Found: As, 22·3. $C_{14}H_{14}O_4NAs$ requires As, 22·4%). The *disodium* salt crystallised from dilute alcohol in glistening leaflets, $p_H$ 9 (Found: As, 19·4. $C_{14}H_{12}O_4NAsNa_2$ requires As, 19·7%).

The work described above was carried out as part of the programme of the Chemistry Research Board, and is published by kind permission of the Director of Chemical Research and the Department of Scientific and Industrial Research. Sincere thanks are also due to the Director for helpful criticism and advice.

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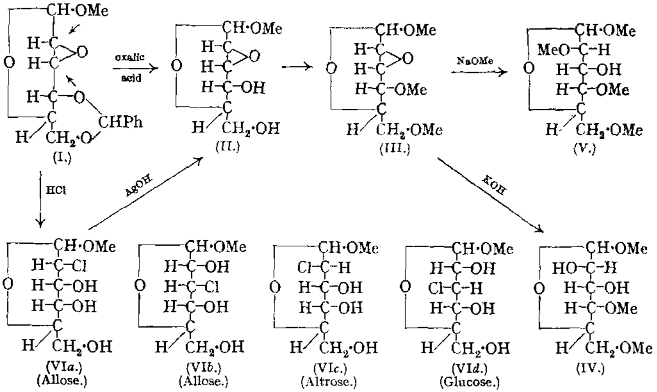
## 97. *The Preparation of 4:6-Dimethyl Altrose and 2:4:6-Trimethyl Altrose from Glucose.*

BY GEORGE J. ROBERTSON and HELEN G. DUNLOP.

The starting point in this research was 4 : 6-benzylidene 2 : 3-anhydro-α-methylalloside (I). Attempts to remove the benzylidene residue by hydrolysis with very dilute hydrochloric acid in acetone solution led to the production of two isomeric *α-methylhexoside chlorohydrins* to which no definite configuration may yet be ascribed. The removal of the benzylidene residue was ultimately achieved by means of hydrolysis with oxalic acid and the resulting 2 : 3-*anhydro-α-methylalloside* (II) was methylated to give 4 : 6-dimethyl 2 : 3-anhydro-α-methylalloside (III), which, in turn, yielded 4 : 6-*dimethyl α-methylaltroside* (IV) and 2 : 4 : 6-*trimethyl α-methylaltroside* (V) on treatment with aqueous caustic potash and a solution of sodium methoxide respectively.

GLUCOSE was converted successively into 4 : 6-benzylidene α-methylglucoside (Irvine and Scott, J., 1913, **103**, 585; Freudenberg, *Ber.*, 1928, **61**, 1758), 2 : 3-di-*p*-toluenesulphonyl 4 : 6-benzylidene α-methylglucoside (Ohle and Spencker, *Ber.*, 1928, **61**, 2387; Mathers and Robertson, J., 1933, 696), and 4 : 6-benzylidene 2 : 3-anhydro-α-methylalloside (I) (Robertson and Griffith, J., 1935, 1196).




When substance (I) was treated with very dilute hydrochloric acid in acetone solution, it was expected that hydrolysis of the benzylidene residue would take place with the production of 2 : 3-*anhydro-α-methylalloside* (II). The reaction is more profound and, in addition to the removal of the benzylidene residue, the ethylene oxide ring is broken and an atom of chlorine enters the molecule. The product is a crystalline solid, m. p. 117—120°, which is not homogeneous, but from which two isomeric *α-methylhexoside chlorohydrins* have been separated in a pure condition by a tedious process of fractional crystallisation. The formation of a sugar chlorohydrin in the course of such a hydrolysis was first noticed by Müller (*Ber.*, 1934, **67**, 423). One of the new substances separates in small prisms, m. p. 160—162°, $[\alpha]_D^{15^\circ}$ + 113·1° in methyl alcohol, and the other in large prisms, m. p. 136—138°, $[\alpha]_D^{15^\circ}$ + 157·2° in methyl alcohol.

It is clear that the ethylene oxide ring may be opened in two ways as indicated by the arrows, and further that in each case the opening may or may not be accompanied by a Walden inversion. This leads to the theoretical possibility that four isomeric α-methylhexoside chlorohydrins may be formed and these are indexed as (VI*a*), (VI*b*), VI*c*), and (VI*d*). At the moment it is impossible to ascribe a definite configuration to either of our isomeric chlorohydrins and work on this problem continues. It is of interest to note, however, that each of them, on treatment with moist silver oxide, is converted into 2 : 3-anhydro-α-methylalloside (II). Moreover, the possibility that our compounds are oxonium salts may be discounted by the fact that on acetylation they give triacetyl α-methylhexoside chlorohydrins.

The problem of removing the benzylidene residue from 4 : 6-benzylidene 2 : 3-anhydro-α-methylalloside without interfering with the ethylene oxide ring was finally solved by using oxalic acid as the hydrolytic agent, and 2 : 3-anhydro-α-methylalloside (II) was obtained as a crystalline solid, m. p. 105—107°. The substance was then methylated with the Purdie reagents and 4 : 6-dimethyl 2 : 3-anhydro-α-methylalloside (III), m. p. 63—64, was obtained in almost quantitative yield. It proved to be identical with the 4 : 6-dimethyl 2 : 3-anhydro-α-methylhexoside obtained by the alkaline hydrolysis of 2 : 3-

*di-p-toluenesulphonyl 4 : 6-dimethyl α-methylglucoside* (Mathers and Robertson, *J.*, *1933*, *1080*).

Now Robertson and Griffith (*loc. cit.*) have shown that, when 4 : 6-benzylidene 2 : 3-anhydro-α-methylalloside is treated with (a) aqueous caustic potash, and (b) sodium methoxide solution, the products are 4 : 6-benzylidene α-methylaltroside and 4 : 6-benzylidene 2-methyl α-methylaltroside respectively. Reasoning by analogy, treatment of 4 : 6-dimethyl 2 : 3-anhydro-α-methylalloside (III) with (a) aqueous caustic potash and (b) sodium methoxide solution should lead to the production of 4 : 6-*dimethyl α-methylaltroside* (IV) and 2 : 4 : 6-*trimethyl α-methylaltroside* (V) respectively. This proved to be the case.

When (III) was treated with aqueous caustic potash, 4 : 6-dimethyl α-methylaltroside (IV) was obtained in good yield as a very hygroscopic, crystalline substance. The presence of the altrose configuration was proved by methylation to give tetramethyl α-methylaltroside, which was identical with that obtained by Robertson and Griffith (*loc. cit.*). The altrosidic methyl group was removed from (IV) in the usnal way by treatment with N-hydrochloric acid and 4 : 6-*dimethyl altrose* was obtained in fine needles, m. p. 158—160°, $[\alpha]_D^{15°}$ + 102·9° in water, changing to + 64·9° in six hours. The sngar yielded 4 : 6-*dimethyl altrosazone*, m. p. 139—141°, on treatment with phenylhydrazine in acetic acid solution.

In similar fashion treatment of (III) with sodium methoxide solution led to the production of 2 : 4 : 6-trimethyl α-methylaltroside (V), which was obtained as a hygroscopic syrup. Hydrolysis of this substance with N-hydrochloric acid yielded 2 : 4 : 6-*trimethyl altrose* as a pale yellow syrup, $[\alpha]_D^{15°}$ + 79·3° in chloroform. The position of the third methyl group was proved by the conversion of the sugar into 4 : 6-dimethyl altrosazone.

The hydrolysis of 4 : 6-dimethyl α-methylaltroside brings out a point of interest. Robertson and Griffith (*loc. cit.*) have shown that when α-methylaltroside, 2-methyl α-methylaltroside, 3-methyl α-methylaltroside, or 2 : 3-dimethyl α-methylaltroside is submitted to acid hydrolysis the reaction proceeds abnormally and leads to the prodnction of a non-reducing anhydro-compound as the main product (cf. Richtmyer and Hudson, *J. Amer. Chem. Soc.*, 1935, **57**, 1716). Nothing definite could be said concerning the position of the anhydro-linkage in these compounds, but it was suggested that it must involve position 4 or 6. This suggestion is confirmed by the fact that 4 : 6-dimethyl α-methylaltroside is hydrolysed in normal fashion to give a reducing sngar which shows mutarotation.

## Experimental.

*Hydrolysis of 4 : 6-Benzylidene 2 : 3-Anhydro-α-methylalloside with Hydrochloric Acid.*—The material (5 g.) was dissolved in a mixture of acetone (500 c.c.) and 2N-hydrochloric acid (18·5 c.c.) and boiled for 3 hours. After neutralisation with barium carbonate and filtration the acetone was distilled. The aqueous residue was washed with ether to remove benzaldehyde and then taken to dryness under diminished pressure. The dry residue was extracted with warm acetone; the acetone extract, on evaporation, yielded a syrup which, on rubbing with ether, gave 2·5 g. of a crystalline solid, m. p. 117—120°. This material contained chlorine and was shown to be a mixture of two isomeric α-methylhexoside chlorohydrins. The product was dissolved in the minimum amount of hot ethyl alcohol and a first fraction (A) was obtained; the mother-liquor was treated with light petroleum and a second fraction (B) was thus precipitated.

Fraction (A), m. p. 120—150°, was crystallised repeatedly from ethyl alcohol until the m. p. was constant and showed no change on crystallisation from acetone. In this way an *α-methylhexoside chlorohydrin*, m. p. 160—162°, $[\alpha]_D^{15°}$ + 113·1° in methyl alcohol ($c$ = 1·265), was obtained in small prisms (Found : C, 39·8; H, 6·1; Cl, 16·9 $C_7H_{13}O_5Cl$ requires C, 39·5; H, 6·1; Cl, 16·7%).

Fraction (B), m. p. 120—130°, was crystallised repeatedly first from ethyl alcohol–light petroleum, then from acetone–ether, until the m. p. was constant and showed no change on crystallisation from ethyl acetate. In this way an isomeric *α-methylhexoside chlorohydrin*, m. p. 136—138°, $[\alpha]_D^{15°}$ + 157·2 in methyl alcohol ($c$ = 1·646), was obtained in large prisms (Found : C, 39·6; H, 6·0; Cl, 17·0%).

*Alkaline Hydrolysis of the Isomeric α-Methylhexoside Chlorohydrins.*—The hydrolysis was

carried out by means of freshly prepared silver oxide and in each case the product was 2 : 3-anhydro-α-methylalloside. A typical experiment is described. The substance (1 g.) was dissolved in water and boiled with an excess of freshly prepared silver oxide for 9 hours. The reaction liquid was filtered and taken to dryness under diminished pressure. The product was contaminated with colloidal silver, which was removed by extraction with methyl alcohol and filtration through norit. The gelatinous product thus obtained yielded, after several crystallisations from acetone, 2 : 3-anhydro-α-methylalloside, m. p. 105—107°, $[\alpha]_D^{15°} + 153°$ in methyl alcohol (cf. below).

*Acetylation of the α-Methylhexoside Chlorohydrins.*—The material (1·6 g.), a mixture of the isomers, was dissolved in dry pyridine (4 c.c.), and acetic anhydride (4 c.c.) added. After 15 hours, the reaction mixture was poured into water and extracted with benzene. The extract was washed with dilute acid, alkali, and water and dried over anhydrous sodium sulphate, and on removal of the solvent a syrup was obtained. This syrup contained chlorine and on analysis gave the figures required for a *triacetyl α-methylhexoside chlorohydrin* (Found : Cl, 10·5; 0·1158 g. of material required 13·75 c.c. of N/10-KOH. $C_{13}H_{19}O_8Cl$ requires Cl, 10·5%; 0·1158 g. requires 13·69 c.c. of N/10-KOH).

*Partial Hydrolysis of 4 : 6-Benzylidene 2 : 3-Anhydro-α-methylalloside.*—The material (5 g.), prepared as described by Robertson and Griffith (*loc. cit.*), was dissolved in acetone (450 c.c.) and after the addition of an aqueous solution of oxalic acid (15 g. in 50 c.c.) the mixture was boiled for 12 hours. After neutralisation with barium carbonate and filtration the acetone was distilled. At this point a small amount of unchanged starting material (0·5 g.) separated and was removed. The aqueous solution was washed with ether to remove benzaldehyde and evaporated to dryness under diminished pressure. The residue was extracted several times with acetone; the combined extracts, on evaporation, yielded a gelatinous product (2·7 g. or 90% yield). This material was purified with difficulty by repeated crystallisation from acetone and 2 : 3-*anhydro-α-methylalloside* was finally obtained as clusters of needles, m. p. 105—107°, $[\alpha]_D^{15°} + 153°$ in methyl alcohol ($c = 2·058$) (Found : C, 48·3; H, 6·8; OMe, 17·0. $C_7H_{12}O_5$ requires C, 47·7; H, 6·8; OMe, 17·6%).

4 : 6-*Dimethyl 2 : 3-Anhydro-α-methylalloside.*—The above 2 : 3-anhydro-α-methylalloside was methylated six times with methyl iodide and silver oxide, and 4 : 6-dimethyl 2 : 3-anhydro-α-methylalloside was obtained in practically quantitative yield. The substance crystallised from light petroleum in long needles, m. p. 63—64°, $[\alpha]_D^{15°} + 188·0°$ in chloroform ($c = 1·475$), and proved to be identical with the 4 : 6-dimethyl 2 : 3-anhydro-α-methylhexoside obtained by Mathers and Robertson (*loc. cit.*), who record m. p. 63—64°, $[\alpha]_D + 188·9°$ in chloroform ($c = 1·017$).

*Action of Aqueous Caustic Potash on 4 : 6-Dimethyl 2 : 3-Anhydro-α-methylalloside.*—A solution of the substance (5·8 g.) in 5% aqueous potassium hydroxide (225 c.c.) was heated on a steam-bath until the rotation was constant (20 hours) : $[\alpha]_D^{15°} + 174·6° \longrightarrow + 133·9°$, allowing for change in concentration. The solution was saturated with potassium bicarbonate and extracted four times with chloroform; the combined extracts were dried over anhydrous sodium sulphate, filtered, and evaporated to dryness. The product was distilled, b. p. 130—135°/0·5 mm., and 4 : 6-*dimethyl α-methylaltroside* obtained as a syrup which crystallised on standing, $[\alpha]_D^{15°} + 145·7°$ in chloroform ($c = 1·38$). Yield, 4·1 g. The substance is exceedingly hygroscopic and the m. p. could not be determined with accuracy [Found : OMe, 40·35 (after drying at 100° in a vacuum for 8 hours). $C_9H_{18}O_6$ requires OMe, 41·9%].

*Methylation of 4 : 6-Dimethyl α-Methylaltroside.*—The substance required eight treatments with the Purdie reagents to effect complete methylation. 2 : 3 : 4 : 6-Tetramethyl α-methylaltroside was obtained in quantitative yield as a syrup, $n_D^{15°}$ 1·4500, $[\alpha]_D^{15°} + 128·8°$ in chloroform ($c = 1·052$). Robertson and Griffith (*loc. cit.*) record $n_D^{15°}$ 1·4500, $[\alpha]_D^{15°} + 128·3°$ in chloroform ($c = 0·931$) (Found : OMe, 59·9. Calc. : OMe, 62·0%).

*Hydrolysis of 4 : 6-Dimethyl α-Methylaltroside.*—The material (3·6 g.) was dissolved in N-hydrochloric acid (80 c.c.) and boiled in the presence of norit until the rotation was constant (3½ hours) : $[\alpha]_D^{15°} + 139·5° \longrightarrow + 61·7°$, allowing for change in concentration. The solution was neutralised with barium carbonate, filtered, and taken to dryness under reduced pressure. The residue was extracted with chloroform, and the extract, after drying over anhydrous sodium sulphate, evaporated to dryness. The crystalline residue (2·1 g.) was recrystallised from acetone, and 4 : 6-*dimethyl altrose* obtained in fine needles, m. p. 158—160°, $[\alpha]_D^{15°} + 102·9°$ in water ($c = 1·96$), changing to $+ 64·9°$ after 6 hours (Found : OMe, 28·7. $C_8H_{16}O_6$ requires OMe, 29·8%).

*Osazone of 4 : 6-Dimethyl Altrose.*—The sugar (0·8 g.) was heated with a solution of phenyl-

hydrazine (2 g.) in dilute acetic acid at 60° for 3 hours. The solid material which separated on cooling was contaminated with tarry matter, but after crystallisation, first from methyl alcohol and then from ethyl alcohol, 4 : *6-dimethyl altrosazone* was obtained as a yellow crystalline solid, m. p. 139—141° (Found: OMe, 15·7. $C_{20}H_{26}O_4N_4$ requires OMe, 16·1%).

*Action of Sodium Methoxide Solution on* 4 : *6-Dimethyl* 2 : *3-Anhydro-α-methylalloside.*—The substance (5 g.) was dissolved in methyl alcohol (100 c.c.) containing sodium (2·7 g.), and the mixture boiled for 20 hours. After cooling and dilution with water, the reaction mixture was extracted four times with chloroform, and the united extracts, after drying over anhydrous sodium sulphate, were evaporated to dryness. The resulting syrup was distilled and 2 : 4 : *6-trimethyl α-methylaltroside*, b. p. 105°/0·1 mm., $n_D^{15°}$ 1·4580, $[\alpha]_D^{15°}$ + 144·9° in chloroform ($c$ = 1·984), was obtained as a very hygroscopic syrup. Yield, 4·3 g. or 80%. When it was left in contact with air for a short time, its refractive index fell from 1·4580 to 1·4550 (Found: OMe, 49·0. $C_{10}H_{20}O_6$ requires OMe, 52·5%).

*Hydrolysis of* 2 : 4 : *6-Trimethyl α-Methylaltroside.*—The substance (2·05 g.) was dissolved in N-hydrochloric acid (40 c.c.) and boiled until the rotation became constant (3½ hrs.): $[\alpha]_D^{15°}$ + 132° ⟶ + 67·6°, allowing for change in concentration. The solution was neutralised with barium carbonate, filtered, and taken to dryness under diminished pressure. The residue was extracted with chloroform and the extract, after drying over anhydrous sodium sulphate, was evaporated. The resulting syrup was dissolved in ether, filtered, and again taken to dryness; 2 : 4 : *6-trimethyl altrose* was then obtained as a pale yellow syrup, $n_D^{15°}$ 1·4765, $[\alpha]_D^{15}$ + 79·3° in chloroform ($c$ = 1·617). Yield, 1·4 g. (Found: OMe, 40·1 after drying at 100° under reduced pressure for 8 hrs. $C_9H_{18}O_6$ requires OMe, 41·9%).

*Osazone derived from* 2 : 4 : *6-Trimethyl Altrose.*—Treatment with phenylhydrazine acetate, as described in the case of 4 : 6-dimethyl altrose above, yielded a yellow crystalline substance, m. p. 139°, which proved to be 4 : 6-dimethyl altrosazone (m. p. and mixed m. p.).

The authors are indebted to the Carnegie Trust for the grant of a Scholarship which enabled one of them (H. G. D.) to take part in the investigation, and to Principal Sir James C. Irvine for his kind help and interest.

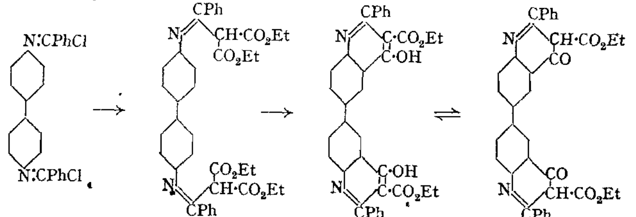
The University, St. Andrews. [*Received, February, 18th*, 1938.]

## 98. *Di-imidochlorides. Part I. Synthesis of Derivatives of 6 : 6′-Diquinolyl and Phenanthroline from Di-imidochlorides.*

By H. K. S. Rao and T. S. Wheeler.

Dibenzbenzididedi-imidochloride on condensation with ethyl sodiomalonate yields a product which gives a derivative of 6 : 6′-diquinolyl on heating. Di-imidochlorides from the benzoyl derivatives of *m*- and *p*-phenylenediamine give phenanthroline derivatives on similar treatment.

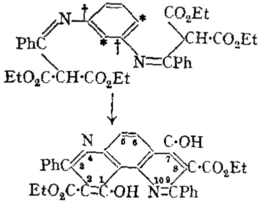
A new diquinolyl (III) synthesis is provided by condensing dibenzbenzididedi-imidochloride (I) (J., 1937, 1643) with ethyl sodiomalonate by Just's method (*Ber.*, 1885, **18**, 2623) as modified by Shah and Heeramaneck (J., 1936, 428) and cyclising the product (II) by heating:




(I.) (II.) (III.) (IV.)

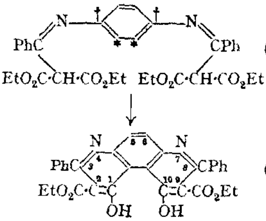
New derivatives of phenanthroline (VI) and $\psi$-phenanthroline (VIII) have been similarly prepared from the di-imidochlorides derived from *m*- and *p*-phenylenediamine respectively (J., 1937, 1643):

(V.)



(VI.)

(VII.)



(VIII.)

These diquinolyl and phenanthroline derivatives have been formulated as hydroxy-compounds, but are probably tautomeric, as is ethyl 4-hydroxy-2-phenylquinoline-3-carboxylate (Heeramaneck and Shah, *Proc. Indian Acad. Sci.*, 1937, **5**, 442). Some part of the water of constitution which the diquinolyl derivatives contain may be attached to the keto-group.

It is assumed by analogy with the Skraup synthesis of phenanthrolines from diamines that cyclisation occurs so that the nitrogen-containing rings have one direct link without an intervening carbon atom (Skraup and Vortmann, *Monatsh.*, 1882, **3**, 570; Smith, *J. Amer. Chem. Soc.*, 1930, **52**, 397). This follows also if one assumes that the cyclisation reaction always involves the ring carbon atom (*) which is doubly linked to the ring carbon atom (†) attached to nitrogen as shown in (V) and (VII).

## Experimental.

*Reaction of Dibenzbenzididedi-imidochloride with Ethyl Sodiomalonate.*—A mixture of the di-imidochloride (4 g.), toluene (20 c.c.), ethyl sodiomalonate (from 2 atoms of sodium), and ethyl malonate (3·5 g.) was refluxed (calcium chloride guard-tube) for 4 hours and diluted with water. Ether extracted an oily product, which on heating for several hours at 100° yielded *NN'-bis-(α-dicarbethoxymethylbenzylidene)benzidine* as a paste. This, crystallised from alcohol, had m. p. 189° (Found: C, 71·2; H, 5·9. $C_{40}H_{40}O_8N_2$ requires C, 71·0; H, 5·9%). When heated at 200—210°, it was converted into *ethyl* 4 : 4'-*dihydroxy*-2 : 2'-*diphenyl*-6 : 6'-*diquinolyl*-3 : 3'-*dicarboxylate*, which after crystallisation from pyridine melted above 300° (Found: C, 69·6; H, 5·2; loss at 160°, 6·0. $C_{36}H_{28}O_6N_2,2H_2O$ requires C, 69·7; H, 5·2; $H_2O$, 5·8%). This ester was hydrolysed by 10% alcoholic sodium hydroxide to the corresponding *acid*, which, being insoluble in most organic solvents, was purified by repeated precipitation from alkaline solution; it had m. p. above 300° (Found: C, 63·3; H, 4·7; loss at 160°, 11·8. $C_{32}H_{20}O_6N_2,4H_2O$ requires C, 64·0; H, 4·7; $H_2O$, 12·0%). The ester was converted, by treatment with hydrochloric acid (1 : 1) in a sealed tube at 170—180°, into 4 : 4'-*dihydroxy*-2 : 2'-*diphenyl*-6 : 6'-*diquinolyl*, which was purified by washing with hot pyridine, alcohol, and acetone, as it was insoluble in all the usual solvents: this may explain the somewhat unsatisfactory analysis, which also gave 0·6% of residue (Found: C, 79·4; H, 4·8; loss at 160°, 4·2. $C_{30}H_{20}O_2N_2,H_2O$ requires C, 78·6; H, 4·8; $H_2O$, 3·9%). The compound melted above 300°.

The condensation products of the di-imidochlorides derived from *m*- and *p*-phenylenediamines with ethyl sodiomalonate were prepared and cyclised to the corresponding phenanthrolines by the method described above.

*NN'-Bis-(α-dicarbethoxymethylbenzylidene)*-m-*phenylenediamine*, crystallised from alcohol, had m. p. 131° (Found: C, 67·9; H, 6·1. $C_{34}H_{36}O_8N_2$ requires C, 68·0; H, 6·0%). *Ethyl* 1 : 7-*dihydroxy*-3 : 9-*diphenylphenanthroline*-2 : 8-*dicarboxylate*, crystallised from alcohol, had m. p. 264° (Found: C, 70·9; H, 4·9. $C_{30}H_{24}O_6N_2$ requires C, 70·8; H, 4·7%). 1 : 7-Dihydroxy-3 : 9-diphenylphenanthroline melted above 300°, but could not be purified, as it separated as a jelly from the usual organic solvents.

*NN'-Bis-(α-dicarbethoxymethylbenzylidene)*-p-*phenylenediamine* melted at 186° (Found: C,

67·8; H, 6·0. $C_{34}H_{36}O_8N_2$ requires C, 68·0; H, 6·0%), *ethyl* 1 : 10-*dihydroxy*-3 : 8-*diphenyl*-ψ-*phenanthroline*-2 : 9-*dicarboxylate* at 218° (Found: C, 70·7; H, 4·8. $C_{30}H_{24}O_6N_2$ requires C, 70·8; H, 4·7%), and 1 : 10-*dihydroxy*-3 : 8-*diphenyl*-ψ-*phenanthroline* above 300° (Found: C, 78·7; H, 4·5. $C_{24}H_{16}O_2N_2$ requires C, 79·1; H, 4·4%). All three compounds were crystallised from alcohol.

The authors' thanks are due to Dr. R. C. Shah for his valuable advice.

Royal Institute of Science, Bombay. [*Received, March 1st*, 1938.]

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## 99. *A Convenient Method for preparing γ-Picoline.*

By G. R. Clemo and W. M. Gourlay.

A method has been worked out for the preparation of the inaccessible γ-picoline from 2 : 4-dimethylpyridine.

Although γ-picoline has been used by a few workers and in particular by Löffler (*Ber.*, 1909, **42**, 124) and Meisenheimer (*Annalen*, 1920, **420**, 190) for the synthesis of quinuclidine, it is generally inaccessible. We have needed it for research purposes for some time and have now worked out a method for its preparation from the easily procurable 2 : 4-dimethylpyridine. When this is treated with benzaldehyde, 2-*styryl*-4-*methyl*- and 2 : 4-*distyryl-pyridine* are formed. These are easily separated by distillation, and oxidation of the former gives the apparently hitherto undescribed 4-*methylpyridine*-2-*carboxylic acid*, which is readily converted into γ-picoline on heating above its melting point. In order to get the best possible yield of γ-picoline in this reaction, conditions would have to be found for reducing the considerable proportion of the distyryl compound now obtained, but even so 2·5 g. can be easily obtained from 10 g. of the lutidine.

### Experimental.

2-*Styryl*-4-*methylpyridine and* 2 : 4-*Distyrylpyridine*.—2 : 4-Dimethylpyridine (12 g.), freshly distilled benzaldehyde (24 g.), and acetic anhydride (24 g.) were refluxed for 16 hours. The mixture was acidified with dilute hydrochloric acid (1 : 1), steam-distilled to remove the excess of benzaldehyde, and made alkaline with sodium hydroxide; after standing, the resulting solid was collected, washed with water, and dried. On distillation 11—12 g. passed over at 160—165°/1 mm., leaving 6·5 g.* in the flask. When the distillate was redistilled, almost the whole passed over at approximately 160°/1 mm. and set to a solid (m. p. 62°). Its *picrate* was sparingly soluble in acetic acid and acetone and separated in yellow prisms, m. p. 258° after slight softening (Found: C, 56·6; H, 3·95. $C_{14}H_{13}N,C_6H_3O_7N_3$ requires C, 56·6; H, 3·8%). The *base* regenerated from the picrate by alkali crystallised from light petroleum in colourless prisms, m. p. 70° (Found: C, 85·9; H, 6·3. $C_{14}H_{13}N$ requires C, 86·1; H, 6·7%). The residue*, which distilled at 250°/1 mm., was crystallised from benzene and then from alcohol, colourless prisms of the *distyryl* compound being obtained, m. p. 172—173° (Found: N, 5·1. $C_{21}H_{17}N$ requires N, 4·9%).

4-*Methylpyridine*-2-*carboxylic Acid*.—The above mono-condensation product (10 g.) was dissolved in acetone (100 c.c.), cooled in ice, and stirred while finely powdered potassium permanganate (20·5 g.) was added during 30 minutes. The reaction mixture was filtered, and the precipitate washed with acetone and extracted three times with hot water (about 60 c.c. each time). The aqueous filtrate was acidified with hydrochloric acid and after 1 hour the precipitated benzoic acid (3 g. approx.) was collected, and the filtrate warmed and stirred while copper carbonate (4·3 g.) was added. The blue copper salt was collected, washed with water, suspended in hot water, and treated with hydrogen sulphide. The filtrate was at once rapidly evaporated to dryness under reduced pressure; the *acid* * (4·5—4·8 g.) was then obtained as a colourless or very slightly coloured solid. It crystallised from benzene in colourless prisms, m. p. 136—137° (Found: C, 61·7; H, 5·2; N, 10·5. $C_7H_7O_2N$ requires C, 61·3; H, 5·1; N, 10·2%). The *ethyl* ester was obtained by dissolving the above crude acid * (4·8 g.) in absolute alcohol (40 c.c.), cooling the solution in ice, and saturating it with dry hydrogen chloride. Colourless crystals soon began to separate, but they had almost all dissolved after 20 hours

at room temperature. The mixture was then refluxed for 1¾ hours, the alcohol removed under reduced pressure, concentrated aqueous potassium carbonate added, and the liberated ester extracted with ether and dried over potassium carbonate; distillation gave the ester (3·95 g.) as a colourless liquid, b. p. 105°/1 mm. (Found: C, 65·4; H, 6·4. $C_9H_{11}O_2N$ requires C, 65·5; H, 6·6%). The ester *picrate* separated from alcohol in well-defined prisms with solvent of crystallisation, which was lost on drying on the water-bath; the picrate then crystallised from benzene in yellow prisms, m. p. 126—127° (Found: C, 46·0; H, 3·3. $C_9H_{11}O_2N,C_6H_3O_7N_3$ requires C, 45·7; H, 3·6%).

*γ-Picoline.*—The crude acid (4·5 g.*) was divided into two portions and each was heated somewhat above its m. p. in a distilling flask with a trace of copper powder for 1 minute and then distilled. γ-Picoline (2·1 g.), which passed over, was redistilled over solid potassium hydroxide and obtained as a colourless liquid, b. p. 142—143°, which gave a picrate, m. p. 166—167°, as described in the literature (Found: C, 44·3; H, 3·0. Calc.: C, 44·7; H, 3·1%), and a *methiodide*, large colourless flat prisms, m. p. 149—150°, from acetone (Found: C, 35·7; H, 4·7. $C_7H_{10}NI$ requires C, 35·7; H, 4·3%).

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NEWCASTLE-UPON-TYNE.

[*Received, March 1st, 1938.*]

## 100. *The Phenazine Series. Part VII. The Pigment of* Chromobacterium Iodinum; *the Phenazine Di-*N*-oxides.*

By G. R. CLEMO and H. MCILWAIN.

The pigment of *Chromobacterium iodinum* (nov. sp.) has been isolated and shown to be the NN′-*dioxide* of a dihydroxyphenazine (probably the 1 : 2-dihydroxy-derivative). Other derivatives of the hitherto unknown *phenazine di*-N-*oxide* (IV) have been prepared, and their reactions studied.

THIS new species of *Chromobacterium* was isolated at the National Institute for Research in Dairying, Reading, during milk examination. The name *Chromobacterium iodinum* was proposed on account of a violet, copper-glinting pigment occurring outside the organism at the later stages of its growth. Cultures, and an account of the examination of the organism carried out at Reading, were sent by Mr. J. G. Davies, to whom our thanks are due; we are also indebted to Prof. Dunlop of the Department of Bacteriology, King's College, for growing several batches of the organism, from which was extracted the pigment used in the present investigation.

The bacteria were grown on a solid agar medium, and after about 15 days had attained maximal pigmentation; the colouring matter was removed by washing with water and extraction with chloroform, and, on concentration of the extract, separated as uniform crystals, deep purple in colour and with coppery lustre, in a yield of about 1 g. per sq. m. of medium. Analytical data indicate for the pigment an empirical formula $C_{12}H_8O_4N_2$; it is not sufficiently soluble in camphor to permit the determination of molecular weight by Rast's method. Its homogeneity is indicated by the fact that, though not adsorbed by sugar or chalk, the pigment gives a single sharp narrow band on alumina. It is not basic, being insoluble in acids except concentrated sulphuric acid, but is soluble in sodium hydroxide, giving a brilliant blue solution which deposits green crystals of the sodium salt. This deposit can be seen under the microscope to dissolve transitorily in water to a rich blue solution, which almost immediately deposits purple crystals of the original pigment; such salt formation and hydrolysis indicate how the pigment, insoluble in water, could be deposited outside the bacterial cell. Alkaline solutions of the pigment are reduced by hyposulphite, the colour changing through red to yellow; the last stage only is reversible by air or by persulphate oxidation. The pigment and its reduction product are precipitated from their alkaline solutions by excess of bicarbonate or sulphur dioxide.

The pigment was shown to be a phenazine derivative by zinc dust distillation of its reduction product, which yielded phenazine itself. The formula $C_{12}H_8O_4N_2$ is that of a tetrahydroxyphenazine; of these compounds, the 1 : 2 : 3 : 4-derivative and a methyl

homologue are known (Kehrmann and coll., *Ber.*, 1887, **20**, 324, 3150; 1888, **21**, 1227; 1890, **23**, 2448) and are consistently described as yellow-brown needles. As various tri-, di-, and mono-hydroxyphenazine derivatives are also yellow, the pigment is not likely to be a simple hydroxyphenazine, though it is phenolic in character.

The action of acetic anhydride is not simple acetylation; it leads to a product whose analytical figures indicate loss of oxygen during the process.

The reduction of the pigment (best in alcoholic solution with platinum and hydrogen) leads to the replacement of two oxygen atoms by two of hydrogen—such as, for example, $-NO_2 \rightarrow -NH_2$, but no product of biological origin has yet been obtained with a nitro-group—and the compound produced, $C_{12}H_{10}O_2N_2$, is readily converted on recrystallisation into $C_{12}H_8O_2N_2$. Such facile dehydrogenation would be expected to occur with an *NN'*-dihydrophenazine and the somewhat high molecular weight recorded is understandable on account of association as in the case of pyocyanine. The reduction product is still phenolic; it gives a green coloration with ferric chloride in alcoholic solution, and forms a diacetyl derivative. Its alcoholic solution gives with lead acetate an intense violet lake which closely resembles that given by alizarin; quinizarin under similar conditions gives no lake. Catechol gives a colourless precipitate and quinol none with alcoholic lead acetate.

In the search for phenomena comparable with these results, the observations of Wohl on phenazine *N*-oxide (*Ber.*, 1901, **34**, 2442; 1903, **36**, 4140) were encountered. This compound yields *NN'*-dihydrophenazine on reduction and phenazine itself on refluxing with acetic anhydride; it is not, however, markedly coloured. The above results of degradation, and also the observed decomposition of the pigment with vigorous gas evolution on melting, would be explained were it a di-*N*-oxide. Such compounds have not been described in the phenazine series; indeed *N*-oxides have never been made directly from the corresponding phenazines, Wohl's product being obtained by heating aniline and nitrobenzene in the presence of sodium hydroxide, and substituted compounds being prepared by Bamberger and Ham (*Annalen*, 1911, **382**, 82) by condensation of *p*-substituted nitrosobenzenes.

In attempts to prepare a di-*N*-oxide, phenazine was recovered unchanged from the action of hydrogen peroxide or benzoyl peroxide in neutral solution (compare Bamberger and Tschirner, *Ber.*, 1899, **32**, 342, 1882; Meisenheimer, *Ber.*, 1926, **59**, 1848), but with Caro's acid (Bamberger and Rudolf, *Ber.*, 1902, **35**, 1082) or, better, with hydrogen peroxide in glacial acetic acid, a product different from the Wohl *N*-oxide, crystallising in orange-red needles, m. p. (with gas evolution) 204°, was obtained. The analytical data corresponded to a *di*-N-*oxide* (IV) and from the products of its thermal decomposition phenazine mono-*N*-oxide and phenazine were obtained.

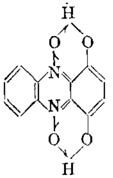
The *di-N-oxide* produced similarly from 1-hydroxyphenazine prepared by the method of Wrede (*Z. physiol. Chem.*, 1929, **177**, 177) shows great similarity to the natural pigment. It is deep red, and forms in alkalis blue solutions which are reduced by hyposulphite irreversibly to red (the colour of the salt of 1-hydroxyphenazine) and further, reversibly, to yellow (the colour of the alkaline salt of 1-hydroxydihydrophenazine). The phenazine *N*-oxides have, in common with other *N*-oxides and with the pigment, the property of liberating iodine from potassium iodide in acid solution. This occurs to only a very small and readily distinguishable extent with phenazine itself, which is partly reduced in the process. It has not yet been found possible to reconvert into the pigment the dihydroxyphenazine formed on its reduction; this may be compared with the greater difficulty of oxidation of 1-hydroxyphenazine in comparison with phenazine, and the lower yield of dioxide obtained.

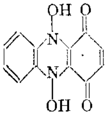
The configuration of the dihydroxyphenazine obtained on reduction has not yet been definitely established. Two acetoxyphenazines, the 2 : 3- and 2 : 6-, have been described, but are different from that isolated from the pigment.

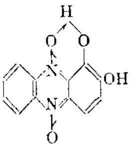
Fischer and Hepp (*Ber.*, 1890, **23**, 8141) and Ullmann and Mauthner (*Ber.*, 1902, **35**, 4305) claim to have prepared 2 : 3-dihydroxyphenazine and its diacetoxy-derivative. We find their dihydroxy-derivative, which gives no lake with alcoholic lead acetate, gives a bright yellow solution in sodium hydroxide, and although their diacetoxyphenazine melts

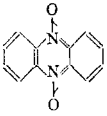
at 230°, its m. p. is depressed to 210—215° by the diacetoxyphenazine from the pigment. Eight other dihydroxyphenazines are possible. The following evidence is brought forward in this connection. Oxidation of the dihydroxydihydrophenazine is complete after the absorption of 10 atoms of oxygen; as oxidation with the conversion of one homocyclic ring into two carboxyl groups requires 8 atoms of oxygen, whereas similar oxidation of the other ring in addition would require 17 atoms, this result is taken to indicate the presence of both hydroxyl groups in the same benzene nucleus of the phenazine skeleton, but so far quinoxaline-2 : 3-dicarboxylic acid has not been isolated from the reaction.

The pigment is insoluble in boiling water, whereas a dihydroxyphenazine is somewhat soluble and phenazine di-*N*-oxide is more soluble in water than phenazine. Similarly 1-hydroxyphenazine di-*N*-oxide is less water-soluble than 1-hydroxyphenazine itself. These results would appear to indicate some interaction between the hydroxyl and the *N*-oxidic oxygen atom, such as by co-ordination in (I), or possibly by tautomerism as in (II), both forms being possible in a 1 : 4-derivative.


(I.)

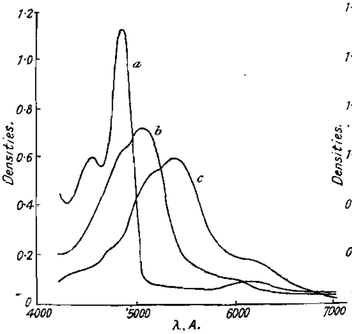

(II.)


(III.)


(IV.)

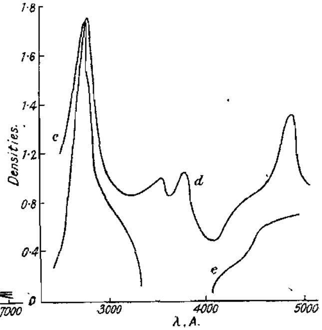
The absorption spectra of 1/100,000 w/v chloroform solutions of phenazine di-*N*-oxide, 1-hydroxyphenazine di-*N*-oxide, and the pigment in the visible region are shown

FIG. 1.




a—*Phenazine di-*N*-oxide.*
b—*1-Hydroxyphenazine di-*N*-oxide.*
c—*Chromobacterium iodinum.*

FIG. 2.




d—*Chromobacterium iodinum.*
e—*Reduction product of pigment.*

in Fig. 1, where it is seen that the action of the 1-hydroxy-group in lowering the extinction coefficient, shifting the absorption maximum to the red, and broadening the band is carried still further by the two hydroxyl groups of the pigment. The 2-hydroxy-compound is unfortunately not at present available for comparison, but the absorption spectrum of the

pigment resembles that of alizarin and not that given by quinizarin. Ultra-vio absorption spectra of the pigment and its reduction product are given in Fig. 2.

Further, chloroform solutions of the pigment and of alizarin scarcely fluoresce ultra-violet light, whereas that of quinizarin gives an intense fluorescence.

The conclusion is reached, therefore, that the pigment is probably 1 : 2-*dihydrox phenazine di*-N-*oxide* (III) and this is being put to the test of synthesis.

The phenazine compounds which have been isolated from natural sources are nc three in number (pyocyanine, chlororaphine, and the present pigment), and, though all a bacterial pigments, phenazine compounds have been shown to exhibit biological activi in a variety of organisms (Friedheim, *J. Exper. Med.*, 1931, **54**, 207), tissues (Friedhei *Biochem. J.*, 1934, **28**, 173; Young, *J. Biol. Chem.*, 1937, **120**, 659; Dickens, *Biochem.* J 1936, **30**, 1064, 1233), and enzyme systems (Green, Stickland, and Tarr, *Biochem. J.*, 193 **28**, 1812; Weil-Malherbe, *ibid.*, 1937, **31**, 2080). It is anticipated that phenazi derivatives, possibly *N*-alkyl compounds (cf. Dickens, Weil-Malherbe), will be found mu more widely distributed in nature. The present pigment is not itself readily reversib oxidised and reduced, and is regarded as related to some compound of functional val to the bacterium.

## Experimental.

*Extraction of the Pigment.*—The bacteria had been grown in medicine bottles lying on the broad sides, each thus affording a surface of beer-wort-agar of 110—120 sq. cm. Th cultures were incubated at 30° for 5 days and then allowed to lie at room temperature f 7—9 days, during which a deep purple layer of coppery lustre developed. Water (20 c.c was added to each, the bottle shaken, and the resultant suspension removed by decantatio Two, or occasionally three, such operations were sufficient to remove the pigment. Th washings were allowed to stand, and the suspension of bacteria decanted from the precipitate pigment, which was further washed in the same manner and extracted with chloroform. C concentration, the *pigment* separated as purple crystals retaining the coppery glint; it wa recrystallised from chloroform; the m. p., 236° (decomp.), was unchanged by further crystal isation. The chloroform mother-liquors contained a relatively small amount of non-pigmente material. The average yield was 10 mg. per bottle, or about 1 g./sq. m. of medium.

Qualitative tests showed the pigment to contain nitrogen; sulphur, phosphorus, and meta were absent (Found: C, 58·9, 59·1; H, 3·3, 3·5; N, 11·6, 11·6. $C_{12}H_8O_4N_2$ requires C, 59·0; H 3·3; N, 11·5%).

The pigment (0·5 mg.) dissolved in glacial acetic acid to a red solution, which on warmi with the addition of 10% potassium iodide solution (0·1 c.c.) liberated iodine, readily detecte by its coloration with starch. The compound, after being refluxed for 3 hours in methy alcoholic potassium hydroxide, was precipitated unchanged by sulphur dioxide.

*Reduction.*—The pigment (0·1 g.), platinum oxide (0·2 g.), and absolute alcohol (10 c.c were shaken in hydrogen (100 lb./sq. in.) for 24 hours. Filtration removed the catalyst, but n organic matter: this, considering the small solubility of the pigment in alcohol, indicate completion of the reaction. The filtrate, concentrated to crystallisation, yielded fine old-gol plates (0·06 g.), m. p. on rapid heating in a sealed tube, 260° (Found: C, 67·5, 67·7; H, 4· 4·7; N, 13·4; *M*, 245. $C_{12}H_{10}O_2N_2$ requires C, 67·3; H, 4·7; N, 13·1%; *M*, 214). When th *substance* was recrystallised from alcohol or ethyl acetate, yellow prisms were obtained, m. p 273—274° (Found: C, 67·9, 67·3; H, 3·8, 3·8. $C_{12}H_8O_2N_2$ requires C, 67·9; H, 3·8%). Th same *compound* was obtained when the pigment was refluxed for 15 hours with an alcoholi solution of *o*-phenylenediamine in a test for the presence of an ortho-quinonoid grouping.

*Acetylation of the Reduction Product.*—The compound (10 mg.) was refluxed for 1 hour ir pyridine (1 c.c.) and acetic anhydride (4 drops), the solvent removed under reduced pressure and the residue crystallised from alcohol; light yellow needles separated, m. p. 234° [Found C, 64·5; H, 4·6; N 9·7. $C_{12}H_6O_2N_2(CO{\cdot}CH_3)_2$ requires C, 64·8; H, 4·1; N, 9·5%]. The *compound* is not soluble in cold dilute acids, but with cold dilute sodium hydroxide hydrolysi occurs slowly, giving a pink solution.

*Conversion into Phenazine.*—The reduction product (10 mg.) was ground with zinc dust (2 g.) and placed in a hard-glass tube with a layer of zinc dust on top; this was strongly heated, and the heating then extended to the mixture. On the cold part of the tube there collected an almost colourless, crystalline sublimate (2 mg. approx.), which crystallised from light petroleum in very pale yellow prisms, m.p. 171°, not depressed by authentic phenazine.

*Phenazine Di-N-oxide.*—Phenazine (0·9 g.) in glacial acetic acid (50 c.c.) and hydrogen peroxide (5 c.c. of 100 vol.) were heated at 50° for 16 hours; the solution, which had then become a richer yellow, was diluted with an equal volume of hot water. On cooling, the *dioxide* separated in fine orange-red needles, which were washed with water and dried at 50° (1·0 g.). Chloroform extraction of the basified (sodium carbonate) mother-liquor yielded a little more (0·1 g.). The whole was recrystallised from alcohol (600 c.c.), yielding orange needles, m. p. 204° (gas evolution) after browning at 150° or lower according to the rate of heating (Found: C, 67·8, 68·2; H, 3·9, 3·6. $C_{12}H_8O_2N_2$ requires C, 67·9; H, 3·8%).

1-*Hydroxyphenazine Di*-N-*oxide.*—1-Hydroxyphenazine (0·5 g.) in glacial acetic acid (20 c.c.) and hydrogen peroxide (2 c.c. of 100 vol.) were heated at 50° for 24 hours. The solution had become rich red, and no further apparent change took place in the course of 24 hours; addition of excess of sodium bicarbonate produced a red sludge. This was collected and extracted with aqueous sodium hydroxide, the resulting blue solution treated with sulphur dioxide, and the red precipitate collected, dried, and crystallised from chloroform–methyl alcohol (1 : 2), 1-*hydroxyphenazine di*-N-*oxide* separating in deep red prisms, with a metallic sheen, m. p. (gas evolution) 189—190° (Found: C, 62·5; H, 3·5. $C_{12}H_8O_3N_2$ requires C, 63·1; H, 3·5%).

*Decomposition of Phenazine Di-*N-*oxide.*—(1). The dioxide (0·1 g.) was refluxed with acetic anhydride (2 c.c.); it gradually dissolved and the solution had become yellow-brown in 10 minutes. It was concentrated to crystallisation; phenazine mono-*N*-oxide, which separated in yellow prisms, was recrystallised from alcohol (0·07 g.; m. p. 223°, alone or mixed with material prepared by the method of Wohl). On longer refluxing, the decomposition to phenazine described by Wohl took place.

(2). When the dioxide (0·1 g.) was heated at 180°, it became brown, phenazine (0·04 g.) sublimed, and an alkali-soluble material was also produced.

One of us (H. McI.) is indebted to the Department of Scientific and Industrial Research for a maintenance grant during the early part of this investigation, and our thanks are due to Mr. W. A. Campbell for making the micro-analyses.

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Newcastle-upon-Tyne, 2. [*Received, February 9th*, 1938.]

## 101. *The Methylation of Triphenylcarbinol.*

By H. H. Hatt.

Triphenylcarbinol is methylated by methyl alcohol in presence of hydrogen chloride, but not by the pure alcohol alone. An addition *compound* of the carbinol and alcohol is described. Triphenylmethyl methyl ether is dimorphous.

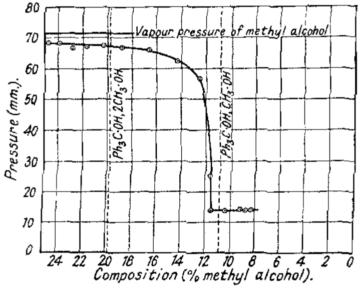
Strauss and Hüssy (*Ber.*, 1909, **42**, 2177) reported that triphenylcarbinol is methylated by boiling with methyl alcohol. In syntheses of tertiary carbinols where a Grignard reagent has been used, the part formation of the methyl or ethyl ether has been sometimes reported (Haller and Guyot, *Bull. Soc. chim.*, 1904, **31**, 979; Thiele and Balhorn, *Ber.*, 1904, **37**, 1463; Stadnikoff, *Ber.*, 1924, **57**, 5). Ether formation may have been due in such cases to subsequent use of an alcohol as a solvent for the carbinol (compare Boyd and Hatt, J., 1927, **904**). In the one case of triphenylcarbinol the conditions under which methyl alcohol can effect methylation have now been more exactly determined.

Triphenylcarbinol was crystallised repeatedly from benzene. The methyl alcohol used was freed from acetone with iodine and alkali, dried with sodium, fractionated repeatedly through a Clarke and Rahrs column (*Ind. Eng. Chem.*, 1923, **15**, 401), and fractionally distilled from sulphanilic acid in a Pyrex apparatus. This alcohol did not methylate triphenylcarbinol. After a solution of the carbinol in methyl alcohol had been refluxed for 100 hours, methylation did not exceed 0·4% (the experimental limit). Methylation also did not occur when the carbinol (1 g.) was refluxed for 5 hours with 0·00001M-methyl-alcoholic hydrogen chloride (10 c.c.), but like treatment with a 0·0001M-hydrogen chloride brought about 83—85% methylation. (This is the equilibrium value reached when these quantities of carbinol and alcohol are used with the hydrogen chloride from 0·0001 to 1·0M:

$$CPh_3{\cdot}OH + CH_3{\cdot}OH \rightleftharpoons CPh_3{\cdot}O{\cdot}CH_3 + H_2O$$

The same equilibrium position is reached by refluxing together corresponding quantities of triphenylmethyl methyl ether, methyl alcohol, and water in presence of hydrogen chloride. The methylations were carried out in Pyrex apparatus. When the methyl alcohol was not distilled from sulphanilic acid, or was stored in soft-glass containers, the catalytic effect of the hydrogen chloride could not be detected below a molarity of 0·0003. The quantity of hydrogen chloride present remained essentially constant during a methylation if its initial molarity did not exceed 0·005; with greater molarities, losses, probably due to evaporation or methyl chloride formation, became appreciable. The extent of methylation was estimated as follows: The reaction mixture was poured into an excess of water, washed in with pure methyl alcohol, rendered alkaline with baryta water, and evaporated several times with water to expel the alcohol. The residues were extracted in benzene, the solvent removed on a water-bath under reduced pressure, and the methoxyl content of the residues estimated by the Zeisel method.

Triphenylcarbinol and methyl alcohol form an addition *compound*, which separates from methyl alcohol in large (1 cm.) colourless rhombs (Found: $CH_4O$, 10·8. $C_{19}H_{16}O,CH_4O$ requires $CH_4O$, 10·9%). The alcohol is lost rapidly at 100°. The results of vapour-pressure measurements of triphenylcarbinol–methyl alcohol mixtures at 15° are shown in the figure.




*Vapour Pressures of Methyl Alcohol-Triphenylcarbinol Mixtures at* 15°.

Clearly, only one addition compound is formed. Its free energy of formation at 15° from solid triphenylcarbinol and liquid methyl alcohol, calculated from its vapour pressure (14 mm.) and that of methyl alcohol (71·3 mm.), is about 930 cals. Thus the hydrogen bridges which here presumably unite the two alcohols possess a considerable stability.

The experience of Norris and Cresswell (*J. Amer. Chem. Soc.*, 1933, **55**, 4946) concerning triphenylmethyl methyl ether has been confirmed. At first this ether was obtained melting at 82·5—83°. In later preparations it was obtained in colourless plates, m. p. 96·0—96·5° (Found: $O{\cdot}CH_3$, 11·3. Calc. for $C_{19}H_{15}{\cdot}O{\cdot}CH_3$: $O{\cdot}CH_3$, 11·3%). All my previous preparations now had this melting point and the lower-melting form could not be obtained. Mr. A. Pilgrim obtained the low-melting form again by working in another laboratory and it was found to change rapidly into the high-melting form upon inoculation. Triphenylmethyl methyl ether is therefore dimorphous, the form of m. p. 83° most frequently obtained being the less stable.

Although pure methyl alcohol cannot methylate triphenylcarbinol in absence of acid, published evidence indicates that this is possible in the case of malachite-green base (Fischer, *Ber.*, 1900, **33**, 3356; Herzig and Wengraf, *Monatsh.*, 1901, **22**, 601).

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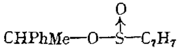
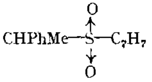
# 102. *The Molecular Rearrangement of (−)Phenylmethylcarbinyl* dl-p-*Toluenesulphinate.*

By C. L. Arcus, M. P. Balfe, and J. Kenyon.

A further study has been made of the molecular rearrangement of (−)phenylmethylcarbinyl *dl-p*-toluenesulphinate to *dl-p*-tolyl-α-phenylethylsulphone (Kenyon and Phillips, J., 1930, 1676). Experiments upon *dl*-phenylmethylcarbinyl *p*-toluenesulphinate show that the rearrangement is facilitated in formic acid solution. The rearrangement of the (−)ester in formic acid solution gives the *dl*-sulphone in 75% yield. The hypothesis of Kenyon and Phillips (*loc. cit.*) that the rearrangement occurs *via* ionisation is confirmed with respect to the greater proportion of the sulphone produced, and is elaborated in the light of the results of experiments on the mutarotation of the ester in solvents. In formic acid solution containing sodium formate a mixture of (−) and *dl*-sulphone is produced, but the yield is only 10%, the main product being a mixture of (−) and *dl*-phenylmethylcarbinyl formate. Both these products have the same relative configuration as the original sulphinic ester. Evidence is adduced that the formate arises (i) as a result of formolysis of the sulphinate, giving the (−)formate, (ii) by combination of α-phenylethyl kations with formate anions, giving the *dl*-formate. It is suggested that the (−)sulphone is formed by intramolecular rearrangement; in the presence of an added anion rearrangement *via* ionisation is diverted and only the small proportion of lævorotatory sulphone formed by the intramolecular process is obtained.

It was suggested (Kenyon and Phillips, *Trans. Faraday Soc.*, 1930, **26**, 451; Kenyon, Phillips, and Taylor, J., 1931, 384) that reactions which result in Walden inversion take place by way of intermediate complex formation whereby the entering anion becomes associated with the asymmetric carbon atom before detachment of the replaced anion is effected, whilst fission of the optically active molecule into a carbonium kation and an anion before the entering anion becomes associated with it results in racemisation. Subsequently, these suggestions were put forward in more precise forms by Polanyi and co-workers (*Z. physikal. Chem.*, 1932, *B*, **19**, 164; 1933, *B*, **20**, 161) and by Hughes, Ingold, and co-workers (J., 1937, 1252).

The second part of this hypothesis, *i.e.*, preliminary fission of the molecule, has been contested on the ground that it would require more energy than is available under the usual conditions of replacement reactions (Wallis and Moyer, *J. Amer. Chem. Soc.*, 1933, **55**, 2598; Olson, *J. Chem. Physics*, 1933, **1**, 418; Olson and Halford, *J. Amer. Chem. Soc.*, 1937, **59**, 2644; Steigman and Hammett, *ibid.*, p. 2540). Hughes and Ingold (J., 1935, 244) considered that solvation of the molecule may provide the energy required for ionisation, whereas Kenyon and Phillips (J., 1930, 1676) concluded that the spontaneous transformation of (−)phenylmethylcarbinyl *p*-toluenesulphinate (I) into *dl-p*-tolyl-α-phenylethylsulphone (II) provided experimental evidence of ionisation during the course of

(I.)   (II.)

the rearrangement. This ionic fission and the racemisation of the liberated kation may be expected to occur more readily in derivatives of α-phenylethane than in those of purely aliphatic secondary alcohols (Hughes, Ingold, and co-workers, *loc. cit.*); it is likely, however, that molecular rearrangement through the intermediate formation of ions is exceptional. For example, Kenyon, Partridge, and Phillips (J., 1937, 207) have provided evidence which suggests that the anionotropic rearrangement of the hydrogen phthalate of α-phenyl-γ-methylallyl alcohol is an intramolecular process. Other investigations (reviewed by Waters, "Physical Aspects of Organic Chemistry," 1935, p. 346 *et seq.*, and by Watson, "Modern Theories of Organic Chemistry," 1937, p. 132 *et seq.*) indicate that intramolecular rearrangement is more common than rearrangement *via* ionisation. If the migrating

*radical is optically active and its asymmetric carbon atom retains its octet of electrons during the rearrangement, asymmetry is completely maintained* (Jones and Wallis, *J. Amer. Chem. Soc.*, 1926, **48**, 169; Wallis and Nagel, *ibid.*, 1931, **53**, 2787; Wallis and Dripps, *ibid.*, 1933, **55**, 1701); intramolecular migration of an optically active radical containing an asymmetric carbon atom carrying a sextet of electrons results in an optically active product with retention of configuration and partial racemisation (Sprung and Wallis, *ibid.*, p. 3838; Wallis and Bowman, *J. Org. Chem.*, 1936, **1**, 383).

In view of its significance and its unique character, the rearrangement of (—)phenylmethylcarbinyl *dl-p*-toluenesulphinate has been submitted to further study. The rearrangement has also been examined of the homogeneous ester, prepared from (—)phenylmethylcarbinol having $\alpha_{5461} - 11{\cdot}9°$ (*l*, 0·25); the ester used by Kenyon and Phillips (*loc. cit.*) was prepared from carbinol of $\alpha_{5461} + 5{\cdot}03°$ (*l*, 0·25). The solid product of the rearrangement, recrystallised once from aqueous ethyl alcohol, gives optically inactive *p*-tolyl-α-phenylethylsulphone in 22% yield.

Table I records the results of experiments using approximately 5 g. of *dl*-sulphinate in 20 c.c. of each of a variety of solvents at laboratory and at elevated temperatures. Col. 2 gives ε, the dielectric constant of the solvent at 20°. The yields recorded are percentages of those obtainable if all the sulphinate had been converted into the derivative in question.

The data in Table I show that decomposition occurs at elevated temperatures. The formation of di-*p*-tolyl disulphoxide during the rearrangement has been discussed by Kenyon and Phillips (*loc. cit.*); *an alternative mode of formation of the disulphoxide is by* the usual decomposition of *p*-toluenesulphinic acid formed, together with styrene, by thermal decomposition of the ester. *p*-Tolyl-α-phenylethylsulphone is stable at 80°, being recovered unchanged after heating at that temperature for 24 hours in the homogeneous state or in nitrobenzene solution. The results of the experiments at room temperature

TABLE I.

*Transformation of* dl-*phenylmethylcarbinyl* dl-p-*toluenesulphinate in solvents and in the presence of sodium formate and sodium* p-*toluenesulphinate.*

| | | Reaction at room temp. | | Reaction at elevated temp. | | |
|---|---|---|---|---|---|---|
| Solvent. | $\epsilon_{20°}$. | Duration, days. | Isolated products.* | Temp. | Duration, hours. | Isolated products. |
| (None) | — | 23 | Sulphone, 27%; styrene, trace | 80° | 3 | Sulphone, 10% (profound decomp.) |
| Ethyl ether satd. with HCl † | — | 18 | Disulphoxide, 22% | — | — | — |
| Benzene | 2·3 | 21 | Sulphone, 9% | 80 | 24 | Disulphoxide, 23% |
| Pyridine | 12·4 | 18 | Unchanged sulphinate | — | — | — |
| Acetone | 21·5 | — | — | 56 | 24 | Unchanged sulphinate |
| Nitrobenzene | 34·1 | 25 | Sulphone, 30% | 80 | 2·5 | Sulphone, 9% (profound decomp.) |
| Acetonitrile | 37·5 | 22 | Unchanged sulphinate | 80 | 20 | Disulphoxide, 21% |
| Formic acid | 57·0 | 22 | Sulphone, 72; formate, 13% | 80 | 2·5 | Sulphone, 54%; formate, trace |
| Sodium formate ‡ in formic acid | — | 23 | Sulphone, 11; formate, 75; sulphinic acid, 12% | — | — | — |
| Sodium *p*-toluenesulphinate § in formic acid | — | 18 | Sulphone, 6; formate, 62% | — | — | — |

* Sulphone, disulphoxide, formate, and sulphinic acid signify respectively *p*-tolyl-α-phenylethylsulphone, di-*p*-tolyl disulphoxide, phenylmethylcarbinyl formate, and *p*-toluenesulphinic acid.

† The sulphinate was recovered unchanged after 20 days from solution in ethyl ether in the presence of anhydrous potassium carbonate, and from ethereal ammonia and ethereal hydrogen chloride.

‡ 2·5 Mols. per mol. of sulphinate. § 1·25 Mols. per mol. of sulphinate

indicate that the rearrangement is favoured in solvents of high dielectric constant, and may be diverted in the presence of added anions; these conclusions are in harmony with the suggestion that the rearrangement occurs *via* ionisation. The comparatively high yield

of sulphone obtained from the rearrangement of the homogeneous sulphinate may be ascribed to the fact that the sulphinate is itself likely to have a high dielectric constant. The difference between the results obtained in nitrobenzene and in acetonitrile solution indicate an unexpected difference in the degree of solvation of the sulphinate in these two solvents, and the facile rearrangement in formic acid solution may be due, not only to the high dielectric constant of this solvent, but also to the ability to solvate both anion and kation, which is peculiar to hydroxylic solvents. If solvation of the kation by formic acid occurs, it must be by electrostatic attraction similar to the hydration of inorganic kations (Day, Hughes, Ingold, and Wilson, J., 1934, 1593), since solvation by co-ordination would result in the formation of phenylmethylcarbinyl formate.

Table II records the products of the rearrangement of the (—)sulphinate, solutions of the same concentrations being used as those described in Table I. The high yield of optically inactive sulphone produced by the rearrangement of the (—)sulphinate in formic acid solution is a convincing confirmation of Kenyon and Phillips's observation that the reaction is accompanied by racemisation.

(—)Phenylmethylcarbinyl formate has the same configuration as the (—)carbinol, because it is converted into this by saponification, a process which does not disturb the bonds of the asymmetric carbon atom (Holmberg, *Ber.*, 1912, **45**, 2997; Ingold and Ingold, J., 1932, 756; Polanyi and Szabo, *Trans. Faraday Soc.*, 1934, **30**, 508). The (—)formate therefore has the same configuration as the (—)sulphinate, which is formed from the (—)carbinol by a reaction in which the bonds of the asymmetric carbon atom are not disturbed. The formation of a mixture of (—) and dl-*phenylmethylcarbinyl formate* during the rearrangement of (—)phenylmethylcarbinyl *p*-toluenesulphinate in the presence of sodium formate cannot be accounted for by any of the hypotheses previously advanced to explain retention of configuration during replacement reactions, *viz.*, occurrence of an even number of consecutive inversion reactions, or the retention by the carbon atom of its electron octet (Kenyon and Phillips, *Trans. Faraday Soc.*, *loc. cit.*), or an intramolecular replacement in which the entering atom and the atom which it replaces are held on the same side of the

TABLE II.

*Rearrangement of (—)phenylmethylcarbinyl* dl-p-*toluenesulphinate in formic acid solution and in the presence of sodium formate and sodium* p-*toluenesulphinate.*

(Optically active products all formed with retention of configuration.)

| | Solvent. | Formic acid. | | $H\cdot CO_2Na$ in $H\cdot CO_2H$. | | Sodium *p*-toluene-sulphinate in $H\cdot CO_2H$.* |
|---|---|---|---|---|---|---|
| | Product. | Sulphone.† | Formate. | Sulphone.† | Formate.‡ | Formate. |
| Crude product | Yield, % | 75 | trace | 13 | — | — |
| | M. p. | 127—130° | — | 110—115° | — | — |
| Purified product | Yield, % | 60 | — | 10 | 75 | 62 |
| | M. p. | 134° | — | 127—128° | — | — |
| | Rotatory power § | nil | — | −65·6° | −9·5° | −0·47° |
| | % of max. recorded rotatory power | nil | — | 63 | 20 | 1 |

* (—) + *dl*-Sulphinate having 75% of maximum rotatory power was used in this experiment. The solid reaction product contained a high proportion of disulphoxide, which made purification of the sulphone difficult.

† The *dl*-sulphone has m. p. 134°, and sulphone of $[\alpha]_{5461}$ +103° in chloroform (*l*, 2·0; *c*, 0·6) has m. p. 124—125° (Kenyon and Phillips, *loc. cit.*).

‡ (—)Phenylmethylcarbinyl formate has $\alpha_{5461}$ −48·90° (*l*, 0·236).

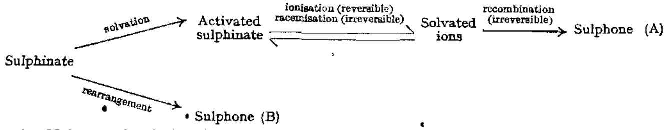
§ $[\alpha]_{5461}$ of the sulphone in chloroform (*l*, 2·0; *c*, 2·65); $\alpha_{5461}$ of the formate (*l*, 0·236).

asymmetric carbon atom (Hughes, Ingold, and co-workers, *loc. cit.*). Sulphinic esters of optically active alcohols, however, undergo reactions analogous to the saponification or alcoholysis of carboxylic esters, in which the bonds of the asymmetric carbon atom are not disturbed. For example, (—)phenylmethylcarbinyl *p*-toluenesulphinate undergoes alcoholysis in ethyl-alcoholic solution (Kenyon and Phillips, J., 1930, *loc. cit.*) with complete retention of configuration. Like sodium acetate in acetic acid solution (Steigman and Hammett, *loc. cit.*), a solution of sodium formate in formic acid is basic, resembling aqueous

*sodium hydroxide in that it contains sodium ions, anions in equivalent amount, and the undissociated acid corresponding to these anions. It can therefore react with the sulphinic* ester *in the* same way that aqueous sodium hydroxide reacts with ethyl (+)α-*p*-toluenesulphinoxypropionate (Gerrard, Kenyon, and Phillips, J., 1937, 153) yielding (—)phenylmethylcarbinyl formate without disturbance of the bonds of the asymmetric carbon atom and therefore uncontaminated by the (+)ester. At the same time the *dl*-formate is produced by the interaction of liberated phenylmethylcarbinyl kations with formate anions. The sum of these two processes is the formation of the mixture of (—) and *dl*-formate with $\alpha_{5461}$ — 9·52° (*l*, 0·236). Since the optically pure ester has $\alpha_{5461}$ — 48·90° (*l*, 0·236), it is concluded that approximately 20% of the formate is optically active and produced by "formolysis," and the remainder is produced from the liberated and immediately racemised carbonium kations. This suggestion is supported by the results of the experiment in formic acid solution in the presence of sodium *p*-toluenesulphinate (Table II). Formate ions are present in this solution, as is shown by the high yield of formate (62%) compared with the low yield of formate in formic acid alone (Tables I and II). The formate produced, however, is almost entirely racemic, because the reaction (formolysis) which results in the formation of optically active formate is repressed by the presence of its products, *p*-toluenesulphinyl ion or *p*-toluenesulphinic acid.

The observations described above support the suggestion that the rearrangement occurs to a preponderating extent *via* ionisation, but the formation of lævorotatory, instead of racemic, *p*-tolyl-α-phenylethylsulphone in 10% yield during the rearrangement of the sulphinate in the presence of sodium formate shows that a small part of the rearrangement can occur by an alternative route. The (—)sulphone has the same relative configuration as (—)phenylmethylcarbinol, because it can be obtained from the latter by two successive reactions, each of which involves inversion of configuration, *viz.*, conversion of the (—)carbinol into the (+)chloride (Kenyon, Phillips, and Taylor, *loc. cit.*) and conversion of this into the (—)sulphone (Kenyon and Phillips, J., 1930, *loc. cit.*). The (—)sulphone has therefore the same configuration as the (—)sulphinate, which is prepared from the (—)carbinol by esterification with *p*-toluenesulphinyl chloride. Like the (—)formate, described above, the (—)sulphone cannot be derived from the (—)sulphinate by replacement reactions. It is therefore concluded that the mixture of (—) and *dl*-sulphone is formed by intramolecular rearrangement, with retention of configuration and partial racemisation, like the rearrangements described by Sprung and Wallis (*loc. cit.*) and Wallis and Bowman (*loc. cit.*). In this type of rearrangement, an optically active product is obtained because the carbonium kation does not become free; fission of the carbon–oxygen bond and formation of the carbon–sulphur bond occur simultaneously. This process was suggested by Wallis and Moyer (*J. Amer. Chem. Soc.*, 1933, **55**, 2598) as the mechanism of the Hofmann rearrangement. If all the (—) + *dl*-sulphone obtained in formic acid–sodium formate solution is produced by intramolecular rearrangement, approximately 15% of the (—)sulphinate undergoes the intramolecular process under these conditions; the racemic fraction of the sulphone obtained may, however, be derived in part from α-phenylethyl kations which fail to react with formate ions.

It is likely that the rearrangement of the sulphinate *via* ionisation is usually accompanied by a minor intramolecular rearrangement. The optically active sulphone is more soluble than the racemic form (Kenyon and Phillips, *loc. cit.*) and, by recrystallisation, a racemic product would therefore be obtained from a sulphone of very low rotatory power. The original explanation of the rearrangement may now be extended as follows:




A = Major reaction, ionic, with racemisation. B = Minor reaction, intramolecular, with retention of configuration.

Support for the above scheme is given by observations of the mutarotation of solutions of the (−)sulphinate in formic acid solution, in which the rearrangement takes place most readily, and in acetonitrile solution, in which it does not occur. The results are given in Table III. The rotatory power of the solution in formic acid (*l*, 0·5) falls from $\alpha_{5461}$ − 3·92°, 20 minutes after dissolution ($\alpha_{5461}$ − 6·7° extrapolated to zero time), to $\alpha_{5461}$ − 0·90° after 75 minutes, but only a small amount (approximately 10% yield) of phenylmethylcarbinyl formate is formed during this time, the rest of the sulphinate being recovered and having, after isolation from the solution, $[\alpha]_{5461}^{17°}$ − 61·7° in ethyl alcohol (*l*, 2·0; *c*, 1·2); the original sulphinate had $[\alpha]_{5461}^{20°}$ − 84·3° (*l*, 2·0; *c*, 5·13). The mutarotation, which is therefore not due to racemisation or to reaction of the sulphinate, and is too rapid to be reasonably ascribed to variation of the specific rotatory power of the sulphinate as a result of its diminished concentration, must be caused by a reversible modification in the environment of the asymmetric carbon or sulphur atoms of the sulphinate molecule, occurring in solution. It can therefore be ascribed to an incipient disturbance of the molecule, prior to ionisation, corresponding to the stage described as solvation in the above scheme. Solvation in this sense implies, not only the attraction of solvent molecules by the solute, but also enhanced reactivity of the solute and formation of a new structure. Evidence of the second stage of the ionic mechanism, reversible ionisation accompanied by racemisation, is given by the observation that the sulphinate recovered from solution in formic acid after 75 minutes has lost 25% of its rotatory power. The third stage of this mechanism is established by the formation of *dl*-sulphone.

The solution of the (−)+ *dl*-sulphinate in acetonitrile, on the other hand, remains unchanged in rotatory power, $\alpha_{5893}$ − 9·46° (*l*, 2·0; *c*, 18·6), during 88 hours. The sulphinate recovered from this solution after 23·5 hours has $[\alpha]_{5461}^{17.5°}$ − 70·3° in ethyl alcohol (*l*, 2·0; *c*, 4·88); the original sulphinate had $[\alpha]_{5461}^{20°}$ − 70·5° in ethyl alcohol (*l*, 2·0; *c*, 5·02). These observations are in harmony with the fact that in this solvent the rearrangement does not take place. The subsequent decrease in rotation is due to the general instability of sulphinic esters, resulting in decomposition and racemisation. After 256 hours the rotatory power of the solution falls to $\alpha_{5893}$ − 4·24° and the sulphinate recovered from the solution at that time has $[\alpha]_{5461}$ − 43·6° in ethyl alcohol (*l*, 2·0; *c*, 4·88).

In ethereal solution in the presence of potassium carbonate the sulphinate shows even greater stability. A solution of the (−)+ *dl*-ester in ether, having $\alpha_{5461}^{17°}$ − 21·52° (*l*, 2·0; *c*, 11·4) when freshly prepared, undergoes little change in rotatory power when kept over anhydrous potassium carbonate during 20 days, $\alpha_{5461}^{17°}$ being then − 21·26°. The sulphinate is recovered from this solution with undiminished rotatory power. The lævorotatory sulphinate undergoes mutarotation in formic acid solution in the presence of sodium formate and sodium *p*-toluenesulphinate, and in nitrobenzene solution (Table IV), but the results cannot be precisely interpreted because certain of the products formed under these conditions are optically active.

TABLE III.

*Mutarotation of solutions of lævorotatory phenylmethylcarbinyl* dl-p-*toluenesulphinate in formic acid and in acetonitrile.*

| In $H\cdot CO_2H$ (*l*, 0·5; *c*, 23·9). | | In $CH_3\cdot CN$ (*l*, 2; *c*, 18·6). | | | | | |
|---|---|---|---|---|---|---|---|
| Mins. after dissolution. | $\alpha_{5461}^{18°}$. | Hours after dissolution. | $\alpha_{5893}^{17°}$. | Hours after dissolution. | $\alpha_{5893}^{17°}$. | Hours after dissolution. | $\alpha_{5893}^{17°}$. |
| 20 | −3·92° | 0 | −9·46° | 42·5 | −9·45° | 160 | −7·62° |
| 40 | −2·41 | 1·5 | −9·44 | 88 | −9·50 | 193 | −5·91 |
| 75 | −0·90 | 11·25 | −9·46 | 112 | −9·25 | 208·5 | −5·34 |
| | | 23·5 | −9·44 | 136·75 | −8·57 | 256 | −4·24 |

EXPERIMENTAL

(−)Phenylmethylcarbinol was prepared by the method of Houssa and Kenyon (J., 1930, 2260), and *dl*- and (−)-phenylmethylcarbinyl *p*-toluenesulphinates by that of Kenyon and Phillips (*loc. cit.*). The (−)sulphinate had $n_D^{17°}$ 1·5745; $[\alpha]_{5461}^{20°}$ − 87·0°, $[\alpha]_{4358}^{20°}$ − 150·2° (*l*, 2·0; *c*, 4·725) in ethyl alcohol.

*Transformation of* dl-*Phenylmethylcarbinyl* dl-p-*Toluenesulphinate*.—(i) *In the homogeneous state.* (a) At room temperature. The *dl*-ester (15·4 g.) after 26 days at room temperature was converted into a crystalline mass which was washed with light petroleum and ethyl alcohol. The residue (5·7 g.), m. p. 110—115°, was twice recrystallised from aqueous ethyl alcohol; the *p*-tolyl-*dl*-α-phenylethylsulphone (2·7 g.) obtained had m. p. 133—134°, alone or mixed with an authentic specimen. From the concentrated light petroleum and alcoholic wash-liquors, an oil (0·5 c.c.), b. p. 45—60°/16 mm., $n_D^{20°}$ 1·518, was isolated, which resinified on addition of a drop of concentrated sulphuric acid and was presumably styrene.

From another specimen of the sulphinate (0·63 g.) the sulphone (0·17 g.) was isolated after 23 days, with m. p. and mixed m. p. 131—133°.

(b) At 80°. The sulphinate (8 g.), when heated on the steam-bath for 3 hours, was converted into a brown crystalline mass from which, by the method described above, 0·8 g. of sulphone, m. p. and mixed m. p. 134°, was obtained.

(ii) *In ethereal solution.* (a) In ethyl ether saturated with hydrogen chloride. A solution of the *dl*-ester (5 g.) in 17 g. of ether saturated with hydrogen chloride, after standing at laboratory temperature for 18 days, was washed with aqueous sodium bicarbonate and with water and dried. The solid residue left after removal of the ether was washed with ethyl alcohol. The solid product (0·6 g.), after recrystallisation from ethyl alcohol, gave di-*p*-tolyl disulphoxide, m. p. and mixed m. p. 78°. From the alcoholic wash-liquor a fraction (2 c.c.), b. p. 76°/22 mm., was obtained, which was presumably α-phenyldiethyl ether (b. p. 67°/14 mm.) formed by interaction of α-phenyl-α-chloroethane with ethyl alcohol.

(b) In ether containing hydrogen chloride (0·7%). A solution of the *dl*-ester (4·4 g.; $n_D^{17°}$ 1·5753) in 25 c.c. of ether containing 0·18 g. of hydrogen chloride was washed as above, after standing at room temperature for 21 days. The residue left after removal of the ether consisted of unchanged ester ($n_D$ 1·564).

(c) In ether containing ammonia (0·1%). A solution of the *dl*-ester (5 g.; $n_D^{17°}$ 1·5753) in 25 c.c. of ether containing anhydrous ammonia (0·025 g.), after standing at laboratory temperature for 21 days, was washed with water and dried. The sulphinate ($n_D^{16°}$ 1·5713) was recovered on removal of the ether.

(d) In ether in the presence of anhydrous potassium carbonate. The *dl*-ester (5 g.; $n_D^{16°}$ 1·5756), after standing for 18 days in ether (20 c.c.) with anhydrous potassium carbonate, was recovered unchanged ($n_D^{16°}$ 1·5740).

(iii) *In benzene solution.* (a) At room temperature. The sulphinate (5 g.; $n_D^{17°}$ 1·5736) was dissolved in benzene (25 c.c.). After 21 days, the benzene was removed and the pasty residue washed with a mixture of light petroleum and ethyl alcohol and recrystallised from aqueous ethyl alcohol. The product (0·45 g., m. p. 132—133°), recrystallised from aqueous ethyl alcohol, gave the *dl*-sulphone, m. p. and mixed m. p. 134°. The light petroleum–ethyl alcohol washings contained 3·8 g. of an oil, which could not be distilled and was presumably sulphinate.

(b) At 80°. The *dl*-ester (6 g.) in benzene (20 c.c.) was heated under reflux for 24 hours, and the benzene then removed by distillation. The solid product was filtered off from the liquid product, and after recrystallisation from alcohol, had m. p. 70—75° (yield 0·75 g.); a second recrystallisation gave di-*p*-tolyl disulphoxide, m. p. (and mixed m. p. with an authentic specimen) 76—77°. From the liquid product (2 c.c.) a few drops were obtained on distillation at 12 mm., bath temp. 150° (αα′-diphenyldiethyl ether has b. p. 154—155°/15 mm.).

(iv) *In pyridine solution.* A solution of the sulphinate (5 g.; $n_D^{16°}$ 1·5756) in pyridine (20 g.), after standing at room temperature for 18 days, was diluted with benzene, washed with dilute hydrochloric acid and with water, and dried (calcium chloride). The benzene was removed by distillation (finally at 15 mm.); the residual oil was unchanged sulphinate, $n_D^{16°}$ 1·570.

(v) *In acetone solution at* 56°. A solution of the *dl*-sulphinate (9·8 g.; $n_D^{15°}$ 1·5761) in acetone (33 g.) was heated under reflux for 24 hours. After removal of the acetone by distillation (finally at 15 mm.), the unchanged ester was recovered, $n_D^{16°}$ 1·562.

(vi) *In nitrobenzene solution.* (a) At room temperature. A solution of the *dl*-ester (5 g.) in nitrobenzene (20 g.), after standing at room temperature for 25 days, was heated at 90°/12 mm. until the solvent was removed. The solid residue was washed with alcohol, leaving a crystalline solid (1·85 g., m. p. 121—128°) from which the *dl*-sulphone (1·5 g.; m. p. and mixed m. p. 134°) was obtained by recrystallisation as described above.

(b) At 80°. A solution of the *dl*-sulphinate (5 g.) in nitrobenzene (20 g.) darkened when heated on the steam-bath for 2·5 hours. The nitrobenzene was removed at 130°/65 mm.; from the dark viscous residue the sulphone (0·4 g., m. p. and mixed m. p. 132—134°) was obtained by recrystallisation from aqueous ethyl alcohol.

(vii) *In acetonitrile solution*. (a) At room temperature. A solution of the sulphinate (5 g.; $n_D^{17°}$ 1·5736) in acetonitrile (15 g.), after standing at room temperature for 22 days, was diluted with ether–benzene, washed with sodium bicarbonate solution and water, and dried, and the solvents removed by distillation (finally at 15 mm.). The residue of unchanged ester had $n_D^{18°}$ 1·568: it remained liquid after standing for 24 hours at − 2°, and after inoculation with sulphone and sulphoxide.

(b) At 80°. A solution of the sulphinate (5 g.) in acetonitrile (20 g.) was heated on the steam-bath for 20 hours, and the solvent removed by distillation at 30 mm. The residual oil after two days deposited crystals of di-*p*-tolyl disulphoxide (0·55 g.), m. p. 80°, which after recrystallisation from alcohol had m. p. and mixed m. p. 79°.

(viii) *In formic acid solution*. (a) At room temperature. A solution of the sulphinate (10 g.) in anhydrous formic acid (40 g.), after standing at room temperature for 22 days, was diluted with ether–benzene (1 : 1) and washed with aqueous sodium bicarbonate (no precipitate was formed on acidifying the wash-liquors). The solvents were removed by distillation; the solid residue (7·2 g., m. p. 129—132°), recrystallised from aqueous alcohol, gave the sulphone (6·1 g), m. p. and mixed m. p. 134°. The wash-liquors yielded *dl*-phenylmethylcarbinyl formate, b. p. 94—95°/20 mm., $n_D^{18°}$ 1·5054 (0·7 c.c. approx.).

(b) At 80°. A solution of the sulphinate (7·4 g.) in formic acid (21 g.) was heated on the steam-bath for 2·5 hours, then poured into water and extracted with ether–benzene. The extract was washed with sodium carbonate solution, dried (calcium chloride), and concentrated. The crystalline residue (4·0 g.), recrystallised from aqueous alcohol, gave the sulphone (3·5 g.), m. p. and mixed m. p. 134°. Distillation of a small amount of oil separated from the solid prodnct gave a few drops, b. p. 90°/20 mm. (phenylmethylcarbinyl formate has b. p. 87°/13 mm.).

(ix) *In formic acid solution in the presence of sodium formate*. A solution of the sulphinate (15 g., 1 mol.) and anhydrons sodium formate (10 g., 2·5 mols.) in anhydrous formic acid (78 g., 30 mols.), after standing at room temperature for 23 days, was diluted with ether–benzene (1 : 1), washed with aqueous sodium bicarbonate, dried (sodium sulphate), and the solvents removed. The residue was separated into a crystalline and a liquid fraction. The former (1·6 g., m. p. 133°), recrystallised from aqueous alcohol, gave the sulphone (1·4 g.), m. p. and mixed m. p. 134—135°; and the latter on distillation gave 6·2 c.c. of material, b. p. 90—91°/16 mm., $n_D^{19°}$ 1·5048, from which on redistillation, dl-*phenylmethylcarbinyl formate*, b. p. 88—88·5°/16 mm., $n_D^{18°}$ 1·5056, $d_{4°}^{13°}$ 1·058, was obtained (Found: C, 72·1; H, 6·7. $C_9H_{10}O_2$ requires C, 72·0; H, 6·7%).

Acidification of the sodium bicarbonate wash-liquor precipitated *p*-toluenesulphinic acid (1·1 g.), m. p. 86—87° (Found: equiv., by titration with N-aqueous sodium hydroxide, 158. Calc. for $C_7H_7{\cdot}SO_2H$: equiv., 156). Recrystallised from hot water, the acid had m. p. 87—88°, alone or mixed with an authentic specimen.

(x) *In formic acid solution in the presence of sodium* p-*toluenesulphinate*. A solution of the *dl*-ester (7·0 g., 1 mol.) and sodium *p*-toluenesulphinate (dried at 110°; 6·0 g., 1·25 mols.) in anbydrous formic acid (36 g.), after standing at laboratory temperature for 18 days, was diluted with ethyl ether, washed with water and with aqueous sodium carbonate, and dried. After removal of the ether and being washed with light petroleum, the solid residue (1·8 g., m. p. 100—105°) was recrystallised from ether–light petroleum. Two crystal forms which were deposited were separated mechanically and recrystallised separately, giving (*a*) di-*p*-tolyl disulphoxide, which after two crystallisations from ether–light petroleum had m. p. and mixed m. p. 77° (yield, 0·3 g.); (*b*) impure *p*-tolyl-α-phenylethylsulphone, which after two recrystallisations from aqueous alcohol had m. p. 130° (yield, 0·35 g.). From the light petroleum wash-liquor above, *dl*-phenylmethylcarbinyl formate was obtained, which after redistillation had b. p. 94·5°/17 mm., $n_D^{21°}$ 1·5075 (yield 2·5 g.). From the sodium carbonate wash-liquor above, *p*-toluenesulphinic acid (1·8 g.) was obtained on acidification (m. p. 87°).

*Thermal Stability of* p-*Tolyl-α-phenylethylsulphone*.—The sulphone was not discoloured by heating on the steam-bath for 24 hours and its m. p. (133—135°) remained unchanged. The sulphone (0·5 g.) in nitrobenzene (5 c.c.) solution was heated on the steam-bath for 24 hours without discoloration and recovered with unchanged m. p. after removal of the solvent.

*Transformation of* (−) *and* (−) + dl-*Phenylmethylcarbinyl* dl-p-*Toluenesulphinates*.—(i) *Homogeneous*. The (−)ester (2·05 g.), after standing for 27 days at room temperature, was converted into a solid mass, which was washed with ethyl alcohol and with light petroleum. The residue (0·75 g., m. p. 113—117°), recrystallised from aqueous alcohol, gave *dl*-*p*-tolyl-α-phenylethylsulphone (0·45 g.), m. p. 129—131°, optically inactive in chloroform solution (*l*, 2; *c*, 2·07); recrystallised from aqueous alcohol, the sulphone had m. p. 132—133°, mixed m. p. with authentic sulphone 134°.

(ii) *In formic acid solution.* A solution of the (–)ester (4 g.) in anhydrous formic acid (16 g.), after standing at room temperature for 9 days, was diluted with ether–benzene (1 : 1), washed with aqueous sodium bicarbonate, and dried (sodium sulphate), and the solvents removed. The residue was washed with light petroleum. From the crystalline product (3·0 g., m. p. 127—130°), recrystallised from aqueous alcohol, *dl-p*-tolyl-α-phenylethylsulphone (2·4 g.) was obtained, m. p. and mixed m. p. 134°, optically inactive in chloroform solution (*l*, 2·0; *c*, 5·04). From the light petroleum wash-liquor, one drop, b. p. 83°/12 mm. (phenylmethylcarbinyl formate), was obtained.

(iii) *In formic acid solution in the presence of sodium formate.* A solution of the (–)sulphinate (10·4 g., 1 mol.) and anhydrous sodium formate (6·7 g., 2·5 mols.) in anhydrous formic acid (50 g., 27 mols.), after standing for 19 days at room temperature, was diluted, washed, and concentrated as in (ii) above. From the residual oil, on fractional distillation, a fraction (4·3 c.c.) was obtained with b. p. 88·5°/13 mm., $n_D^{16°}$ 1·5066, $\alpha_{5893}^{17°}$ – 7·92°, $\alpha_{5461}^{17°}$ – 9·53° (*l*, 0·236). Redistilled, this fraction was identified as (–) + *dl*-phenylmethylcarbinyl formate, b. p. 91°/15 mm.; $n_D^{17°}$ 1·5056, $\alpha_{5893}^{17°}$ – 8·03; $\alpha_{5461}^{17°}$ – 9·52 (*l*, 0·236). The solid undistillable residue was washed with aqueous alcohol, and the crystalline product (1·4 g., m. p. 110—115°) was twice recrystallised from aqueous alcohol, yielding (–) + *dl-p*-tolyl-α-phenylethylsulphone, m. p. 127—128°, $[\alpha]_{5461}^{16°}$ – 65·6° in chloroform solution (*l*, 2·0; *c*, 2·65). Acidification of the sodium bicarbonate wash-liquor from this preparation precipitated *p*-toluenesulphinic acid (0·7 g.), m. p. and mixed m. p. 86° (Found: equiv., 159).

(iv) *In formic acid solution in the presence of sodium* p-*toluenesulphinate.* A solution of 7·0 g. (1 mol.) of (–) + *dl*-phenylmethylcarbinyl *p*-toluenesulphinate {$[\alpha]_{5461}^{21°}$ – 70·3° in ethyl alcohol (*l*, 1; *c*, 5·1); prepared from (–) + *dl*-carbinol having $\alpha_{5461}^{19°}$ – 19·66° (*l*, 0·5)} and 6 g. (1·25 mols.) of sodium *p*-toluenesulphinate (dried to constant weight at 110°) in anhydrous formic acid (36 g., 27 mols.) was kept at room temperature for 18 days. Table IV records the variation in rotatory power of this solution. At the end of 18 days it was diluted with ethyl ether, washed with aqueous sodium carbonate and with water, and dried (calcium chloride). The solid residue left after removal of the solvent was extracted with light petroleum; the crystalline residue {2·2 g., m. p. 79—105°, $[\alpha]_{5461}^{17°}$ – 5·4° in chloroform (*l*, 2; *c*, 5·01)}, after three recrystallisations from aqueous ethyl alcohol, had m. p. 100—110°, and was optically inactive in chloroform solution. After two further recrystallisations *dl-p*-tolyl-α-phenylethylsulphone (0·15 g.) was obtained, m. p. and mixed m. p. 135°. From the light petroleum extract, (–)+ *dl*-phenylmethylcarbinyl formate was obtained, b. p. 90·5—91°/14 mm., $n_D^{22°}$ 1·5050, $\alpha_{5461}^{21°}$ – 0·47° (*l*, 0·236). Acidification of the sodium carbonate wash-liquor precipitated *p*-toluenesulphinic acid (2·4 g.), m. p. 86°.

(–)*Phenylmethylcarbinyl Formate.*—A solution of (–)phenylmethylcarbinol [4 g., $\alpha_{5461}$ – 11·88° (*l*, 0·25)] in mixed formic–acetic anhydride (7 g.), after heating on the steam-bath for 90 minutes, was diluted with ether, and the solution washed with sodium bicarbonate, with water, and dried over sodium sulphate. After removal of the ether, (–)phenylmethylcarbinyl formate, b. p. 88·5—89·5°/14 mm., was obtained. After redistillation, it had b. p. 87—87·5°/14 mm., $n_D^{18°}$ 1·5048, $d_{4°}^{18°}$ 1·057, $\alpha_{6438}^{20°}$ – 33·04°, $\alpha_{5893}^{20°}$ – 40·57°, $\alpha_{5780}^{20°}$ – 42·66°, $\alpha_{5461}^{20°}$ – 48·90°, $\alpha_{4358}^{20°}$ – 88·6° (*l*, 0·236), whence $[\alpha]_{6438}^{20°}$ – 132·8°, $[\alpha]_{5893}^{20°}$ – 163·0°, $[\alpha]_{5780}^{20°}$ – 171·6, $[\alpha]_{5461}^{20°}$ – 196·5°, $[\alpha]_{4358}^{20°}$ – 356·0°, yield, 4·2 g.

After standing for 11 months in a closed vessel, this formate, which then had $[\alpha]_{5461}^{20°}$ — 185·0° (*l*, 0·236), was saponified by heating on the steam-bath with potassium hydroxide (1·25 mols.) in ethyl alcohol for 30 minutes. The solution was extracted with ether, and the extract washed with aqueous potassium carbonate and dried (potassium carbonate), yielding (—)phenylmethylcarbinol, b. p. 95·5—96°/15 mm., $n_D^{20°}$ 1·5271, $\alpha_{5461}^{20°}$ — 10·90°, (*l*, 0·236).

*Mutarotation of* (–) *and* (–)+dl-*Phenylmethylcarbinyl* dl-p-*Toluenesulphinate in Solution.*—(i) *In formic acid.* The (–)+*dl*-ester of $[\alpha]_{5461}^{20°}$ – 84·3° (*l*, 2·0; *c*, 5·13 in ethyl alcohol), $n_D^{19°}$ 1·5703, was used. The observations of rotatory power of a solution of this ester (1·5 g.) in formic acid (5·8 g.) are given in Table III. After the last observation had been made, the solution was poured into water and extracted with ether. The extract was dried, and the ether removed. From the residue, phenylmethylcarbinyl formate (0·2 c.c.) was obtained, b. p. 86°/12 mm., $n_D^{15°}$ 1·5058, leaving (–)+*dl*-phenylmethylcarbinyl *p*-toluenesulphinate, $n_D^{16°}$ 1·5672, $[\alpha]_{5461}^{17°}$ – 61·7° in ethyl alcohol (*l*, 2·0; *c*, 1·20).

(ii) *In acetonitrile.* (–)+*dl*-Ester of $[\alpha]_{5461}^{20°}$ – 70·5° in ethyl alcohol (*l*, 2·0; *c*, 5·02), $n_D^{20·5°}$ 1·5740, was used. The observations of rotatory power of a solution of this ester (8·7 g.) in acetonitrile (30·2 g.) are given in Table III. 23·5 Hours after the solution was made, a portion was withdrawn, and the solvent removed by distillation, finally at 0·1 mm. The residual ester

TABLE IV.

*Mutarotation of solutions of* (−) *and* (−) + dl-*phenylmethylcarbinyl* p-*toluenesulphinate in nitrobenzene, and in formic acid containing sodium formate and sodium* p-*toluenesulphinate.*

[$l$ = 2·0 except where otherwise indicated. $t$ = Time (hours) after dissolution.]

| (−)Ester in nitrobenzene. | | | | (−)Ester (3·09 g.) in $H{\cdot}CO_2H$ (16·4 g.) with $H{\cdot}CO_2Na$ (2·0 g.). | | (−)Ester (1·96 g.) in $H{\cdot}CO_2H$ (15·2 g.) and $H{\cdot}CO_2Na$ (1·83 g.). | | (−) + *dl*-Ester (7·0 g.) in $H{\cdot}CO_2H$ (36 g.) and sodium *p*-toluenesulphinate (6·0 g.). | |
|---|---|---|---|---|---|---|---|---|---|
| Solution kept at 31°. ($c$, 4·80.) | | ($c$, 17·3.) | | | | | | | |
| $t$. | $\alpha^{17°}_{5893}$. | $t$. | $\alpha^{17°}_{5893}$.* | $t$. | $\alpha^{17°}_{5461}$. | $t$. | $\alpha^{19°}_{5461}$. | $t$. | $\alpha^{18°}_{5461}$. |
| 0·5 | −4·90° | 1 | −2·20° | 0·5 | −16·79° | 0·1 | −12·16° | 45 | −8·70° |
| 20 | −4·59 | 18 | −2·33 | 2·5 | −16·57 | 2·0 | −11·84 | 69 | −7·44 |
| 43 | −0·63 | 66 | −2·34 | 3·75 | −16·46 | 19·5 | −10·76 | 95 | −6·31 |
| 47 | −0·46 | 74 | −2·31 | | | 67·5 | − 9·45 | 118 | −5·60 |
| 66·5 | −0·18 | 90 | −2·27 | | | 75 | − 9·26 | 165 | −4·46 |
| 71·5 | −0·15 | 120 | −2·20 | | | 92 | − 8·93 | 218 | −3·79 |
| | | 140 | −2·15 | | | 122 | − 8·46 | 310 | −2·82 |
| | | 165 | −1·93 | | | 143 | − 8·19 | 381 | −2·47 |
| | | 186 | −1·65 | | | 167 | − 7·90 | 434 | −2·21 |
| | | 234 | −1·31 | | | 188 | − 7·58 | | |
| | | 288 | −0·82 | | | 230 | − 7·32 | | |
| | | | | | | 289 | − 7·00 | | |

* $l$ = 0·25.

had $n_D^{17·5°}$ 1·5752, and $[\alpha]^{18°}_{5461}$ − 70·3° in ethyl alcohol ($l$, 2·0; $c$, 4·88). The ester recovered in the same way after 256 hours had $n_D^{17·5°}$ 1·5740, $[\alpha]^{18°}_{5461}$ − 43·6° in ethyl alcohol ($l$, 2·0; $c$, 4·88); it remained liquid when kept for 24 hours at − 2°.

(iii) *In nitrobenzene*. The observations are given in Table IV. Darkening of the solution prevented observation after 288 hours. The specific rotatory power of the ester in nitrobenzene solution does not vary with concentration sufficiently to affect these results: $[\alpha]^{17°}_{5893}$ − 51·1° ($l$, 2·0; $c$, 4·80), $[\alpha]^{17°}_{5893}$ − 50·5° ($l$, 2·0; $c$, 1·02).

(iv) *In formic acid solution containing sodium formate.* The changes in rotatory power of a solution of the (−)ester in formic acid in presence of 2·5 and of 3·6 molar proportions of sodium formate are given respectively in the third and fourth sections of Table IV. The first solution after 3·75 hours was poured into water and extracted with ether, the extract washed with aqueous sodium bicarbonate, dried, (sodium sulphate), and the ether removed. The residual sulphinate gave no distillate at 130°/13 mm. It had $n_D^{19°}$ 1·5703, and $[\alpha]^{20°}_{5461}$ − 84·3° in ethyl alcohol ($l$, 2·0; $c$, 5·130).

(v) *In formic acid containing sodium* p-*toluenesulphinate*. Table IV gives the change in rotatory power of the solution, the preparation of which is described above.

(vi) *In ether containing potassium carbonate*. The (−) + *dl*-ester {1·76 g., $[\alpha]^{20°}_{5461}$ − 70·5° in ethyl alcohol ($l$, 2·0; $c$, 5·02); $n_D^{20·5°}$ 1·5740} in solution in ether (9·8 g.) with potassium carbonate (0·7 g.) was observed polarimetrically ($l$, 2·0). The original rotation, $\alpha^{17°}_{5461}$ − 21·52°, was maintained, the value after 20 days being $\alpha^{18°}_{5461}$ − 21·26°. Ether was then removed from the filtered solution, finally at 0·1 mm., yielding (−) + *dl*-ester having $n_D^{19°}$ 1·5753, $[\alpha]^{19°}_{5461}$ − 70·8° in ethyl alcohol ($l$, 2·0; $c$, 4·775).

The formic acid used in these experiments was prepared from the 98—100% acid by repeated solidification and partial liquefaction, the fluid being rejected.

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# 103. *A Note on* cyclo*Hexylideneacetic Acid.*

By C. G. Le Fèvre and R. J. W. Le Fèvre.

An interest in the configuration of monocyclic *cyclo*hexane derivatives led us during 1935 to attempt—and fail to effect—the optical resolution of *cyclo*hexylideneacetic acid (A), a result which was entirely consistent with the criticisms levelled by Goldschmidt and Gräfinger (*Ber.*, 1935, **68**, 279), Dey and Linstead (J., 1935, 1063), and Desai and Hunter (*Nature*, 1935, **136**, 608) against the claim (Qudrat-i-Khuda, *J. Indian Chem. Soc.*, 1931, **8**, 277; *Nature*, 1933, **132**, 210; 1935, **136**, 301) that isomerides corresponding to the two multiplanar Sachse forms of the simple *cyclo*hexane ring system were stable and capable of isolation.

$$CH_2{<}^{CH_2\cdot CH_2}_{CH_2\cdot CH_2}{>}C{=}CH\cdot CO_2H$$

(A.)

In the course of our work several alkaloidal salts of (A) have been examined. The use of *Aspergillus versicolor* as a resolving agent has been noted, and comparisons recorded with *A. niger* and a mould of the *Penicillium* species concerning the relative efficiencies in destructive attack on the *l*-configuration of lactic acid.

## Experimental.

cyclo*Hexylideneacetic Acid.*—This was prepared essentially by Wallach's method (*Annalen*, 1906, **347**, 328; 1909, **365**, 261), which we found to give higher yields than that of Hope and Perkin (J., 1909, **95**, 1363), even when the latter was improved by effecting the formation of the ethyl *cyclo*hexylmalonate under pressure. In an endeavour to find a simpler preparation, the following experiment was performed.

*Attempted Perkin Condensation with* cyclo*Hexanone.*—A mixture of the ketone (19 g.), fused sodium acetate (10 g.), and acetic anhydride (30 g.) was heated at 180° for 2 days. The mass was then poured while hot into water and neutralised with sodium carbonate, the oily material removed by steam distillation, and the aqneous solution after clarification acidified with hydrochloric acid and left at 0° overnight. No deposition of *cyclo*hexylideneacetic acid occurred. If the oily distillate were repeatedly shaken with fresh sodium bisulphite solution until free from *cyclo*hexanone, a small quantity of a pleasant-smelling liquid remained unattacked; this was taken up in ether, dried, etc., and had b. p. 180—184°. From its analysis (Found : C, 68·2; H, 8·8%) it appeared probable that the substance was the acetate of the enolic form of *cyclo*hexanone (Mannich, *Ber.*, 1906, **39**, 1594) (requiring C, 68·5; H, 8·6%); this was confirmed by (a) the direct production of *cyclo*hexanone on prolonged alkaline hydrolysis, and (b) the isolation of *cyclo*hexanonesemicarbazone, m. p. 166°, from a mixture of the oil (b. p. 180—184°), alcohol, semicarbazide hydrochloride, and dilute caustic soda solntion which had been kept at room temperature for a few days.

*Attempted Resolution of* cyclo*Hexylideneacetic Acid.*—(a) *Brucine.* The alkaloid hydrochloride (1·798 g.; slightly less than ½ equiv.) was dissolved in the minimum amount of water and mixed with a solution of the acid (1·288 g.) in 0·9203N-sodium hydroxide (10 c.c.). The emulsion formed was induced to crystallise by addition of a few drops of alcohol and scratching. The brucine *salt* was thus obtained as white granular crystals, very soluble in alcohol, chloroform, carbon tetrachloride, but sparingly so in light petroleum; m. p. 55—57° (yield, 1·5 g.) (Found : C, 61·6; H, 7·55. $C_{31}H_{46}O_{10}N_2$ requires C, 61·6; H, 7·7%); 0·3935 g., dissolved in 25 c.c. of absolute alcohol, gave $\alpha_D$ − 0·95° (2·2 dcm.), whence $[\alpha]_D^{18}$ *ca.* − 30° (neutral salts of brucine usually show a specific rotation of this order; cf. Tykosiner, *Rec. Trav. chim.*, 1888, **1**, 148).

(b) *Quinine.* Solutions of quinine hydrochloride dihydrate (1·835 g. in water, 30 c.c.) and the sodium salt of (A) (from the acid, 1·835 g., in water, 30 c.c.) were mixed. In various experiments the solutions were either hot or cold, and were in some instances diluted with water and in some with alcohol. The quinine *salt* separated in most cases after long scratching as a matted mass of microcrystalline needles (about 1·8 g.), m. p. 98—104° (Found for a sample dried in a vacuum desiccator : C, 67·1; H, 7·8. $C_{28}H_{36}O_4N_2,2H_2O$ requires C, 67·2; H, 8·0%); 1·8526 g., dissolved in ethyl alcohol (25 c.c.), gave $[\alpha]_{5463}^{18°}$ − 137°. All specimens of the salt and the filtrates from them were shaken repeatedly with aqueous ammonia and chloroform, etc., as usual and from the ammonium *cyclo*hexylideneacetate solutions so obtained the free acid (A) was precipitated by acidification with dilute hydrochloric acid. No activity was observed.

(c) *Strychnine.* After preliminary trials the following procedure was adopted: The sodium salt from 1·1648 g. of the acid and 10 c.c. of 0·8320N-caustic soda, diluted to 500 c.c. with hot water, was treated with strychnine hydrochloride (1·7 g.) in hot water (100 c.c.). After standing at room temperature for 24 hours, the deposited salt (0·2 g.; m. p. 264—285°) was separated, shaken repeatedly with aqueous ammonia and chloroform, and finally with light petroleum. The aqueous solution of the ammonium salt had $\alpha_D$ − 0·08°, acidification (dilute hydrochloric acid) changed this to $\alpha_D$ − 0·07°, but the acid, m. p. 85—90°, obtained by ether extraction had zero rotation. The filtrate from the strychnine salt was evaporated to half bulk; about 0·4 g. of (A) was obtained on cooling, m. p. 90—92° (alone or mixed with an authentic specimen). Finally, concentration of the solution to *ca.* 100 c.c. gave 0·7 g. of long needles, m. p. *ca.* 280—290°, which were too sparingly soluble in alcohol or acetone to permit an $\alpha$ determination; however, decomposition with 2N-sodium hydroxide and chloroform, etc., eventually led to a sodium salt solution which, like the acid obtained by acidification and ether extraction, showed no optical activity.

(d) *Cinchonine and cinchonidine.* The alkaloid hydrochloride (1·483 g.), dissolved in cold water (90 c.c.), alcohol (10 c.c.), and one drop of dilute hydrochloric acid, was mixed with a solution of the acid (1·165 g.) in 0·8320N-sodium hydroxide (10 c.c.). Glassy oils were formed immediately in both instances; these were separated by decantation and rapidly decomposed with aqueous ammonia and chloroform, the aqueous portions being treated similarly at the same time. In neither of the cases did the solutions, or the specimens of acid recovered from them by acidification and ether extraction, exhibit any detectable optical activity.

*Action of Moulds on* cyclo*Hexylideneacetic Acid and* cyclo*Hexanoneoxime.*—*cyclo*Hexanoneoxime with a *trans* strainless configuration should be an optically resolvable substance. However, all attempts—including the duplication of the methods successfully used for the resolution of camphoroxime (Pope, J., 1899, **75**, 1108; Proc., 1899, **15**, 199)—gave only non-crystallisable gums. We therefore sought to demonstrate the resolvability of the acid and the oxime, and to this end examined the growth of the moulds, *Aspergillus niger*, *A. versicolor*, and a green species of *Penicillium* on aqueous solutions containing these substances as a source of carbon. The experiments were carried out generally as follows: A stock culture solution was made up to the following recipe: water (1 l.), sodium nitrate (2 g.), potassium dihydrogen phosphate (1 g.), potassium chloride (0·5 g.), magnesium sulphate heptahydrate (0·5 g.), ferrous sulphate crystals (0·01 g.). 200-C.c. quantities of this solution were placed in 1 l. Roux culture flasks and sterilised by heating at 130° in an autoclave for 1 hour; when they were cold, about 1 g. of the freshly recrystallised acid or oxime was added, and the solution infected with the mould with the usual precautions and left to incubate at 22° for a few days. When a definite growth of mycelia was noticed, a daily polarimetric examination was made. This was easily performed without altering the horizontal position of the flask or disturbing the carpet of mould by withdrawing 10—15 c.c. of the clear lower liquid through a suitably bent sterilised pipette, stirring it with a little charcoal, and filtering it directly into the polarimeter tube. Growth occurred slowly with the acid, but no perceptible resolution was observed. The oxime appeared to be toxic to the moulds; this action was clearly seen by the addition of a specimen to very strongly growing colonies, *e.g.*, those on media containing glycerol as a carbon source; no further extension or sporing took place.

In later experiments with the acid, ammonium acetate (0·1 g.) was added to the stock culture solution, thus bringing its $p_H$ to 4, with advantageous results on the growth of all three moulds. Small rotations (*ca.* 0·02°) were observed with the solutions containing *A. niger* and *A. versicolor*. Such activities cannot be regarded as significant, however, as they could result from the moulds themselves. Good growths of *A. niger* and the *Penicillium* were secured on a glycerol-containing medium; the mycelia and fruiting hyphæ were separated as cleanly as possible, carefully washed with water, and ground with chalk and water. In both cases the altered extracts were slightly dextrorotatory.

*Note on the Use of* A. Versicolor.—This mould does not appear to have been used for the present purpose, although it commends itself by its apparently omnivorous character (cf. action on paraffin wax; Chibnall and Hopkins, *Biochem. J.*, 1932, **26**, 133). The following investigatory experiment was instituted to estimate its efficiency relative to the other two used in the present work: 12 flasks, each containing 150 c.c. of the previously described stock culture solution (plus ammonium acetate), were divided into four groups. To nine of the flasks sodium lactate (6·5 g.) was added and all 12 were sterilised as above. Three flasks containing sodium lactate and one without were infected with *A. versicolor*; the other two groups of four were similarly infected with the *Penicillium* and *A. niger*. All were placed in an in-

*cubator at 22°. Polarimetric examinations were carried out after good sporing had commenced. The observations tabulated were made after the intervals stated; the angles refer to the rotation given by a column of l = 2·2 dcm.*

| Time, days after infection | 14 | 28 | 30 | 35 | 39 | 42 | 46 |
|---|---|---|---|---|---|---|---|
| *A. versicolor* | −0·02° | −0·12° | −0·14° | −0·17° | −0·08° | −0·07° | −0·05° |
| *A. niger* | — | — | — | −0·02° | −0·03° | — | — |
| *Penicillium* | −0·02° | −0·08° | −0·07° | −0·06° | — | — | — |

Thus it appears (1) that *A. versicolor* can under these conditions attack the lævo-form of lactic acid * more rapidly than can the other moulds, and (2) that with it simultaneous destruction of both antipodes is not so pronounced as it is with the other two.

The authors thank Professor J. C. Drummond for facilities in the Biochemical Department, and Professor H. Raistrick and the Curator of the National Collection of Type Cultures for supplies of the moulds.

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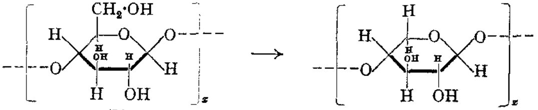
University College, London. [*Received, February 19th*, 1938.]

## 104. *Pectic Substances. Part I. The Araban and Pectic Acid of the Peanut.*

By E. L. Hirst and J. K. N. Jones.

The polysaccharides present in the seeds of *Arachis hypogæa* have been isolated and examined. They include starch, cellulose, and a complex which is shown to be a mixture of pectic acid and araban. After methylation by treatment of the thallium derivative of the complex with methyl iodide, separation can be effected; methylated araban and methylated pectic acid are described. Hydrolysis of the methylated araban gives rise to 2 : 3 : 5-trimethyl arabofuranose, 2 : 3-dimethyl arabinose, and 3-methyl arabinose, the structures of which are proved. Reasons are given for the view that araban contains solely furanose residues, and the molecular structure of the araban, which must contain branched chains, is discussed. The observations are held to throw doubt on the probability of the usually accepted mechanism for the phytochemical derivation of pentosans from hexosans, namely, the direct transformation by oxidation at the sixth carbon atom, followed by decarboxylation.

There has been much speculation concerning the origin of the pentose sugars in nature and the view most generally held is that they are derived from the corresponding hexoses by a process of oxidation at the terminal carbon atom, followed by decarboxylation. For instance, *d*-galactose, *d*-galacturonic acid, and the stereochemically related pentose *l*-arabinose are found closely associated in pectic materials and there is a corresponding structural relationship between the cellulose and the xylan constituents of woody fibres. In the latter instance, the fundamental molecular structures of the hexose and pentose units are similar, being pyranose units linked through the 1 : 4-positions, and it seemed reasonable to imagine that the long chains of xylopyranose residues (II) in xylan had originated by oxidation and decarboxylation from the long chains of the similarly united



(I.) (II.)

glucopyranose units (I) in cellulose. A difference, which may be of fundamental importance, was, however, brought to light by the discovery (Haworth, Hirst, and Oliver,

* In aqueous solution the alkali salts of *d*- and *l*-lactic acid exhibit *l*- and *d*-rotations respectively.

J., 1934, 1917) that the long molecules of xylan were terminated by an arabofuranose residue, this being the first observed occurrence of the arabofuranose structure in products of natural origin. Furthermore, unpublished results obtained by the present writers in the course of work on damson gum show that arabofuranose and galactopyranose residues can occur together in one and the same molecule. It thus becomes all the more necessary to determine the ring structure of the pentose residues present in pectic materials, since it is not possible to derive, by simple oxidation and decarboxylation, a pentose residue containing a furanose structure from a hexopyranose residue. Such a transformation would involve change of ring structure and so far as is known at present no such transformation can occur unless the glycosidic link is broken by hydrolysis and the free sugar liberated. If, therefore, the arabans and the associated polygalacturonides and galactans differ with respect to ring structure or molecular arrangement, doubt will be cast on the validity of the above simple and direct mode of transformation.

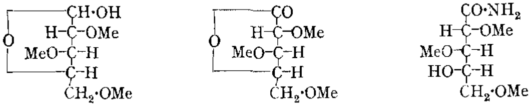
We decided to approach the problem of the phytochemical origin of the pentose sugars by instituting a comparison of the structures of the associated hexose and pentose units present in pectic substances and hemicelluloses. Little information is at present available concerning the detailed molecular constitution of any members of this group. A review of the literature revealed that a close association of *d*-galacturonic acid with *l*-arabinose was found in the seeds of many leguminous plants, the substances in question beiug referred to vaguely as galactoarabans. We selected for a first study the polysaccharides present in the seeds of *Arachis hypogæa* (ground nut; pea-nut). In addition to starch and cellulosic materials, we isolated a complex of pectic acid and araban which was found to be a mixtnre and not a single polysaccharide. In this respect, the observations are of interest in connection with those of recent workers (compare, for example, Schneider and Bock, *Ber.*, 1937, **70**, 1617), who tend to doubt the occurrence of arabinose residues as constituent parts of the pectin molecule. Our results demonstrate that the araban is composed entirely of arabofuranose residues and that the molecular structure comprises branched chains. On the other hand, the associated pectic acid is characterised by very high dextrorotation and by its extreme resistance to acid hydrolysis. It would appear, therefore, to be pyranose in structure and it seems very unlikely that any such simple generic relationship as that mentioned above can exist between the arabinose and galacturonic acid residues which are found together in *Arachis* seeds. Nevertheless, the close stereochemical relationship between *d*-galactose and *l*-arabinose remains significant and it may be that the transformation of a hexosan into a pentosan involves enzymic hydrolysis to single molecules, followed by resynthesis.

The pea-nut meal used as starting material contained some 50% of oil and 25% of protein in addition to carbohydrate material. After removal of the oil and protein the crude carbohydrate mixture was extracted with hot dilute alkali, which dissolved most of the araban–pectic acid complex, leaving the starch and cellulose. More drastic treatment with alkali removed the starch, which was purified by transformation into the acetyl derivative. The constitution of this material and of the cellulose portion will be considered in another communication. The araban–pectic acid complex appeared to be a mixture of the two components, araban and pectic acid, inasmuch as the properties of different samples varied and the components were not present in fixed stoicheiometric proportions and could be separated to some degree by extraction with aqueous alcohol or by fractional precipitation from alkaline solution by acid. Gentle hydrolysis removed the araban completely, leaving the pectic acid unattacked. On the other hand, the araban portion was best separated in a homogeneous condition after partial methylation of the mixture; the araban, which underwent etherification much more readily than the pectic acid, then became easily separable.

The preparation of derivatives of the two polysaccharides proved to be a matter of great difficulty. Methylation by the methods usually successful with polysaccharides resulted in extensive decomposition. New methods had to be sought for, and ultimately success was achieved by using a modification of Menzies's procedure (J., 1926, 937), in which the thallium derivative of a carbohydrate is heated with methyl iodide. A special advantage of this method in the case of polyuronides is that it leads directly to the forma-

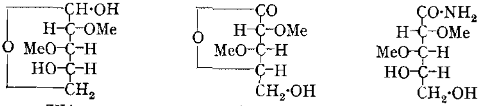
tion of the methyl ester of the methylated product. Two methods of procedure were adopted, designed, as shown in the experimental section, to lead ultimately to the isolation of methylated pectic acid in the one instance and of methylated araban in the other.

The constitution of the pectic acid portion will be considered later and in the present paper we are concerned primarily with the structure of the methylated araban, which was obtained in the fully methylated condition after completion of methylation by the aid of the Purdie reagents. It was an amorphous substance, the analytical data for which corresponded to dimethyl araban. On gentle hydrolysis with methyl-alcoholic hydrogen chloride it gave rise to three products in approximately equimolecular proportions, namely, 2 : 3 : 5-*trimethyl methyl*-l-*arabinoside*, 2 : 3-*dimethyl methyl*-l-*arabinoside*, and 3-*methyl methyl*-l-*arabinoside*. The identity of the first of these was readily proved by its conversion successively into 2 : 3 : 5-trimethyl *l*-arabinose (III), 2 : 3 : 5-trimethyl γ-*l*-arabonolactone (IV), and 2 : 3 : 5-trimethyl *l*-arabonamide (V) (compare Pryde, Humphreys, and Waters, J., 1931, 1298; Haworth, Hirst, and Oliver, J., 1934, 1922).



(III.) (IV.) (V.)

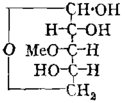
The position of the methyl groups in the dimethyl *l*-arabinose (VI) followed from the following considerations. In the first place, the yields and properties of the *lactone* and *dimethyl* l-*arabonamide* prepared from the dimethyl sugar showed that the product was homogeneous and not a mixture of different dimethyl sugars. The high positive rotation (+ 106°) of the dimethyl sugar itself showed that the sugar could exist in the pyranose form, the rotational differences between pyranose and furanose forms in the arabinose series being by this time well established and so noteworthy that they may be utilised with certainty in assigning ring structures. The lactone (VII) derived from (VI) by bromine oxidation had a strong lævorotation, and this fact, coupled with the extremely slow rate of hydrolysis, established it as a γ-lactone. It follows, therefore, that neither position 4 nor position 5 was occupied by a methyl group and the sugar must therefore be 2 : 3-*dimethyl* l-*arabinose*. Further evidence on this point was secured by the observation that the amide (VIII) failed to give a positive Weerman test when allowed to react with sodium hypochlorite, indicating that position 2 was occupied by a methyl group.



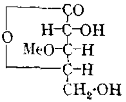
(VI.) (VII.) (VIII.)

The identification of the *monomethyl arabinose* depends on the following observations, and although these do not involve the use of crystalline reference compounds, the results are so clear-cut and definite that there need be no hesitation in assigning the methyl group to position 3. The free sugar possesses the high positive rotation characteristic of pyranose forms in the *l*-arabinose series and its gives a lævorotatory γ-lactone. Positions 4 and 5 therefore contain hydroxyl groups. Furthermore, comparison of the rotations of the sugar and the *lactone* with those of other corresponding derivatives of *l*-arabinose indicate that there can be no appreciable contamination with any methylated arabinose containing methyl groups in either of positions 4 and 5. The *amide* (XI) obtained from the lactone (X) gives a positive Weerman reaction, the yield of product obtained being identical with that given by *l*-arabonamide. Position 2 therefore possesses a hydroxyl group and the one methyl group must be situated at position 3. The yields of lactone and amide,

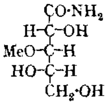
together with the rotational and other evidence, all point to the homogeneity of this monomethyl sugar, and the only structure which will account for the experimental data is (IX).



(IX.)



(X.)

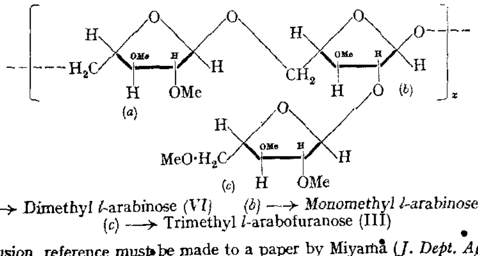


(XI.)

There remains to be discussed the problem of the molecular constitution possible for a methylated araban which gives rise to the above three sugars on hydrolysis. The data so far available are insufficient for the allocation of a unique formula, but the main features of the structure are nevertheless clear. The high viscosity of methylated araban, especially in view of the fact that the molecule is not a straight chain, points to a large molecular size and the initial problem is to combine the three residues represented by the hydrolysis products to give a repeating unit capable of forming, by primary valencies, products of high molecular weight. The residue (III) must be furanose, but (VI) and (IX) by reason of the free hydroxyl groups can be combined in either the pyranose or the furanose form. However, the extreme ease of hydrolysis and the strong lævorotation of araban point to the presence solely of furanose residues united by α-glycosidic links. The trimethyl arabinose must be attached as the terminal unit of a side chain and the simplest interpretation of the facts is obtained by postulatiug a main chain of arabofuranose residues linked through positions 1 and 5, with an arabofuranose residue attached by its reducing group to position 2 of every alternate unit of the main chain, giving the repeating unit shown in (XII) and diagrammatically in (XII *a*). Repeating units of the types shown diagrammatically in (XIII), (XIV), and (XV), or combinations of any of these, would also satisfy the experimental observations. Reference to models shows that (XIV) and (XV) give a highly congested array of atoms, but the structures in question do not seem to be impossible on stereochemical grounds.

With structural units of this type the method of end-group assay for determining chain length or deciding between the possible types of chain is inapplicable, since the termination of the main chain would not necessarily be signalised by the introduction of a new and easily recognisable group, as is the case with methylated cellulose and methylated starch. Conditions are indeed closely similar to those discussed in connection with the structure of yeast-mannan (Haworth, Hirst, and Isherwood, J., 1937, 784). The latter polysaccharide resembles araban in containing a repeating unit composed of three mannose residues, one pair of which must be united by a 1 : 2 link, but differs from araban in that all the mannose units of yeast-mannan are of the pyranose type.

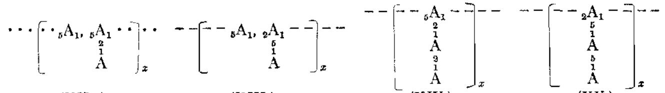
(XII.)



(*a*) ⟶ Dimethyl *l*-arabinose (VI) (*b*) ⟶ *Monomethyl l-arabinose* (IX)
(*c*) ⟶ Trimethyl *l*-arabofuranose (III)

In conclusion, reference must be made to a paper by Miyama (*J. Dept. Agric. Kyushu University*, 1935, **4**, 200), who has described a polysaccharide from peanuts, which appears to resemble closely the araban–pectic acid complex described above, but differs

from it in containing galactose. It is not certain, however, that the material examined by Miyama was homogeneous and he failed to recognise that galacturonic acid residues are an essential structural feature, being of the opinion that the galacturonic acid present was derived by alkaline oxidation of galactose during the process of isolation. This reaction does not take place and a simple explanation of his observations follows from the fact that recovery of the mixed polysaccharides from their solution in alkali results in loss of araban and progressive increase in the uronic acid content of the recovered material. The methods employed by Miyama in allocating structures are invalidated by a misunderstanding of the properties of partly methylated sugars. For example,



(XIIa.) (XIII.) (XIV.) (XV.)

In (XIIa)—(XV), A = an α-arabofuranose residue united to other residues through the numbered C-atoms.

the presence of arabopyranose residues is claimed (*loc. cit.*, p. 220) on the ground that trimethyl arabopyranose is formed on methylation of the hydrolysis products from his methylated polysaccharide. We have shown that such hydrolysis products contain 2 : 3-dimethyl and 3-monomethyl *l*-arabinose, which exist in the polysaccharide as furanose units but revert to the pyranose form on hydrolysis. Methylation of these would lead to the formation of trimethyl arabopyranose, but such a result has no bearing on the ring structure present in the polysaccharide. It is obvious that no serious consideration can be given to structural formulæ advanced on such uncertain and misleading evidence.

## Experimental.

*Extraction of Polysaccharides from Seeds of* Arachis Hypogæa.—The seeds (peanuts) (11 kg.) were dried at 90°/10 mm. for 12 hours. The thin skins had then become brittle and were easily removed by trituration of the nuts in an air blast. The skins were collected for further examination. The nuts were then powdered, and the oil content removed partly by pressure (heated presses should not be employed) and partly by extraction with boiling alcohol (oil content, 45%). The meal was then stirred for 4 hours, with 10% aqueous sodium chloride (40 l.), and the liquid filtered through cloth. After five repetitions of this process the greater part of the protein content (*ca.* 30%) had been removed. The meal was next washed with water and then stirred with boiling 0·2% aqueous potassium hydroxide (20 l.) for 4 hours. After filtration through cloth the liquor was poured into methylated spirits (60 l.) and the precipitate was washed with alcohol and dried in a vacuum at 70°. The extraction of the meal with alkali was repeated two or three times until the polysaccharides isolated gave a faint blue colour with iodine in slightly acid solution. The products (77 g.) which gave no colour with iodine consisted mainly of a complex of pectic acid and araban (material A; see below). Traces of starch may be removed by the action of diastase on a solution of the potassium salt.

The peanut meal was next extracted with boiling 5% aqueous potassium hydroxide (20 l.). The filtered solution was poured into methylated spirits (60 l.), giving a pale yellow solid which consisted mainly of starch contaminated with material (A) and cellulosic material (protein content, nil). The extractions were repeated until the residue gave no colour with iodine. The combined starch fractions (75 g.) were then treated with pyridine and acetic anhydride; the starch went into solution, leaving the other polysaccharides undissolved. After filtration of the solution the acetylated starch was isolated in the usual way ($[\alpha]_D^{20°}$ + 170° in chloroform. Found: $CH_3$·CO, 43%). This was a typical starch acetate and further confirmation of its identity was forthcoming from its quantitative hydrolysis to crystalline glucose.

That portion of the pea-nut meal which resisted the action of boiling 5% alkali solution was mainly cellulose but was contaminated by some non-saponifiable oily material, which was removed by washing successively with alcohol (acidified with acetic acid) and then with ether. The cellulose so obtained (200 g.) gave crystalline glucose in almost quantitative yield on hydrolysis by the method of Monier-Williams. It dissolved in cuprammonium solution

and gave quantitatively on acetylation by the Barnett method a cellulose acetate having $[\alpha]_D^{20°}$ − 10° in chloroform containing 10% of alcohol.

*Properties of the Araban–Pectic Acid Complex.*—This material (A, p. 500) still contained traces of protein and starch. Purification was effected by drying it at 90°/10 mm. until the impurities had become insoluble in water. The solid was then stirred with water, and the flocculent insoluble residue removed in the centrifuge. This residue was washed with water, and the washings added to the aqueous solution of (A). On addition of alcohol a cream-coloured powder was precipitated. This purified potassium salt was redissolved in water, and the araban–pectic acid complex precipitated by addition with stirring of a slight excess of hydrochloric acid. The precipitate was triturated with alcohol until all the hydrochloric acid and potassium chloride had been removed, and finally it was dried at 50°/10 mm.

The araban–pectic acid complex so obtained was a white powder, insoluble in water, but soluble in dilute alkali, giving viscous solutions. It gave no colour with iodine solution or with zinc chloroiodide. Hot concentrated alkali solution caused decomposition, with formation of deep orange-coloured products. The complex had $[\alpha]_D^{20°}$ + 120° (neutral sodium salt, in water, *c*, 1·5, calc. on weight of free polysaccharide). Equiv. wt., 388 (by titration with N/10-sodium hydroxide). N, nil. OMe, nil. (On titration with alkaline iodine under the conditions given by Bergmann and Machemer for determination of iodine numbers, 1·0 g. required 2·6 c.c. of N/10-iodine.) Furfural, 31·7% (estimated both as barbiturate and as phloroglucide, after treatment of the polysaccharide with boiling 12% hydrochloric acid in the usual way). Uronic acid content, from the amount of carbon dioxide liberated on boiling with 12% hydrochloric acid, 45·8%. A substance containing 45·8% of uronic anhydride and no other acidic residues should have an equivalent weight of 383 (Found by titration of A with alkali, 388). Moreover, this proportion of uronic anhydride accounts for 10·1% of the total furfural. This leaves 21·6% of furfural contributed by the pentosan portion of the polysaccharide and since the only pentose present is arabinose (see below) the calculated araban content of (A) is 40·5% (Found: 40%, from estimation of arabinose after hydrolysis). Finally, the equiv. wt. of the pectic acid portion, which was free from araban, was found to be 214 (by carbon dioxide estimation and by direct titration), corresponding to a pectic acid content of 45·8 × 214/176, *i.e.*, 55·7%. Thus the analytical data satisfactorily account for 96·2% of polysaccharide (A).

Hydrolysis of the polysaccharide complex could be effected by boiling an aqueous solution of the substance for 20 hours. The solution darkened owing to decomposition and a little furfural was evolved. The solution was then neutralised with barium carbonate, filtered through charcoal, concentrated under diminished pressure, and poured into alcohol. The barium salt of a polygalacturonic acid was precipitated (yield, 33%) (equiv. wt., by estimation of barium content of salt, 232; furfural, 16·2%). The alcoholic filtrate contained *l*-arabinose, which was obtained, on evaporation of the solvent, in the crystalline condition, m. p. 157—158°, $[\alpha]_D^{21°}$ + 107° (equilibrium value in water, *c* 0·6), diphenylhydrazone, m. p. 202°, characteristic osazone, m. p. 166°. The yield of arabinose diphenylhydrazone actually isolated corresponded to an araban content of 27% and since under the conditions of the experiment pure arabinose gives only 66% of the theoretical yield of diphenylhydrazone the estimated araban content of the polysaccharide was 40%.

When the hydrolysis of the polysaccharide was carried out by heating it at 90° with 1% hydrochloric acid, a definite stage was reached at the end of 3 hours, and on pouring the mixture into alcohol the undissolved material was separated from the arabinose. The insoluble material (a white powder) was free from admixed araban and had all the properties of a pectic acid. Equiv. wt., by titration, 214; $[\alpha]_D^{20°}$ + 224° (as sodium salt in water); it gave typical insoluble calcium and copper salts. The high equivalent weight shows that the substance is not composed entirely of uronic acid residues. We have obtained a pectic acid with the same equivalent weight and properties from strawberry pectin.

Total hydrolysis of the polysaccharide was effected with 3% sulphuric acid at 90° in 30 hours. After neutralisation with barium carbonate the filtered solution was poured into alcohol, and filtered. The filtrate gave arabinose, estimated as the diphenylhydrazone [yield (corr.) corresponds to 40% araban]. No other sugar could be detected. The barium salt gave the characteristic derivative of galacturonic acid with *p*-bromophenylhydrazine, but no glycuronic acid could be detected. Repeated precipitation of the polysaccharide (A) from alkaline solution by dilute acid in the cold resulted in a progressive fall in the equiv. wt. and a corresponding increase in the rotation value. After five such treatments the product had $[\alpha]_D^{20°}$ + 177° (as sodium salt) and equiv. wt. 273. A similar separation was achieved by use of dilute thallium

hydroxide solution, which gave an insoluble derivative with the pectic acid portion and a more soluble one with araban. On removal of the thallium the araban had a strong negative rotation, whereas the recovered pectic acid obtained had properties similar to those recorded above.

These observations indicated that (A) was not a chemical individual but an intimate mixture of pectic acid and araban. Further confirmatory evidence in favour of this view was obtained by extracting (A) with 70% alcohol at 20°. The dissolved material was soluble in water, non-reducing, not precipitatable by acid from aqueous solution, did not contain acidic groups, gave no insoluble copper complex on addition of copper sulphate, no insoluble calcium salt, and had a negative rotation. It was hydrolysed by hot dilute hydrochloric acid with extreme ease, giving only arabinose. The portion insoluble in alcohol showed progressive rise in rotation and fall in equiv. wt. as the extraction proceeded, but the rate of extraction was slow and it was not possible by this means to obtain pectic acid free from adherent araban.

Yet further evidence of the non-homogeneity of (A) is found in the observation that samples prepared from the same supply of pea-nuts showed considerable variation in properties. Some

| Preparation | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| $[\alpha]_D^{20°}$ (as sodium salt) | +120° | + 79° | +140° | +171° | +177° | +224° |
| Equiv. wt. | 388 | 452 | 359 | 292 | 273 | 214 |

typical results are recorded in the accompanying table, preparations (1), (2), and (3) being isolated directly from pea-nut meal. Products (4) and (5) were obtained when (2) was extracted by dilute alkali solution. Preparation (6), obtained by the action of dilute acid on (1), was free from araban and appeared to be composed entirely of pectic acid.

Since the equiv. wt. of the pectic acid portion is 214, it is possible to calculate from the above values the percentage of pectic acid in preparations (1), (2), (3), (4), and (5). If now these values are plotted against the observed rotation values, the latter lie approximately on a straight line. By extrapolation the rotation for araban free from pectic acid is − 50°, which may be regarded as an approximation to the rotation of the araban portion of polysaccharide (A). That this is of the right order of magnitude is shown by the observation (see below) that the fully methylated derivative of araban has $[\alpha]_D^{20°}$ − 90° in methyl alcohol.

When heated with nitric acid (*d* 1·2) under the standard conditions (compare Dorée, " Cellulose Chemistry," 1933 ed., p. 411), polysaccharide (A) gave mucic acid (yield, 21·4%). This confirmed the presence of galacturonic acid residues, but control experiments carried out under similar conditions with pectic acid (from strawberry pectin) and with lactose showed that the yields of mucic acid from combined galacturonic acid and combined galactose derivatives are variable and unreliable for quantitative analysis. Results with free galactose and free galacturonic acid are reproducible (yield in each case, *ca.* 62% of the theoretical), but high and uncertain correction factors are required in the case of polygalacturonides which are resistant to hydrolysis.

*Methylation of the Araban–Pectic Acid Complex: Isolation of Methylated Araban.*—Preliminary experiments showed that methylation of the polysaccharide (A) could not be effected by the usual methods. With methyl sulphate and sodium hydroxide the mixture became dark and no methylated derivative could be isolated. The material was recovered unchanged when the liquid ammonia–sodium–methyl iodide method was used and direct application of the Purdie method was equally unsuccessful.

Methylation was successfully carried ont by a modification of the method employed by Menzies (*loc. cit.*) for the preparation of methyl ethers from the thallium derivatives of hydroxy-compounds. The polysaccharide (30 g.) was allowed to swell under water and to the swollen mass N-thallium hydroxide (450 c.c.) was added with stirring. After 2 hours at 20°, light being excluded, the liquid was filtered, and the solid material washed with alcohol and thoroughly dried at 60°/20 mm., again with exclusion of light. The lemon-yellow solid (98 g., containing 49 g. of thallium titratable with dilute sulphuric acid and phenolphthalein) was powdered and boiled with methyl iodide containing a little anhydrous methyl alcohol. (At this stage complete absence of moisture is essential, and the operation should be carried out in a dim light. It is frequently advantageous to carry out the reaction with methyl iodide under pressure at higher temperatures, in which case thallous oxide or silver oxide is added to the mixture to counteract the possible development of acidity.) After 12 hours the solvent was removed at 30°/10 mm., and the solid mixture of thallium iodide and partly methylated product was mixed with thallium ethoxide (60 g.) in benzene (200 c.c.). After a few minutes' shaking, the benzene was distilled at 30°/10 mm. and the remaining solid was powdered and boiled with methyl iodide with the precautions mentioned above. After removal of the methyl iodide the

product was separated from thallium iodide by solution in boiling methyl alcohol and on removal of the solvent it was obtained as a yellow solid (25·3 g.) (Found: OMe, 30·0%; $[\alpha]_D^{20°}$ + 4° in methyl alcohol, *c* 1·3). This had a higher araban content than the original material (A). Some of the pectic acid remained in the thallium iodide, from which it could be extracted in the form of a partly methylated derivative by means of hot water. The yellow solution was again treated with thallium ethoxide, followed by methyl iodide. The product was separated from thallium iodide by solution in methyl alcohol. It was then treated with ether, giving a soluble portion (B) and an insoluble portion (C). The ether-soluble portion (9·8 g.; $[\alpha]_D^{20°}$ + 6° in methyl alcohol; OMe, 40%) was separated by fractional precipitation into a stiff syrup (D) (7 g.) and a solid (2·7 g.), which was added to the material (C) insoluble in ether. (D) on distillation gave material (3 g.) with b. p. up to 200°/0·001 mm.; $[\alpha]_D$ + 4° in methyl alcohol; OMe, 54%; equiv. wt., *ca.* 140. This reduced neutral permanganate in the cold and rapidly decolorised bromine in carbon tetrachloride. It was similar to products we have obtained by treatment of pectic acid by the above procedure and is obviously composed of oxidised decomposition products.

The ether-insoluble material (C) had $[\alpha]_D^{20°}$ − 31° in methyl alcohol; OMe, 32%; equiv. wt., 800. It was remethylated with methyl iodide and silver oxide, giving a yellow solid (12·5 g.; $[\alpha]_D^{21°}$ − 45° in methyl alcohol; OMe, 37·8%), which was separated by fractional precipitation from chloroform (by addition of light petroleum) into a crisp solid (E) (7·8 g.) and a slightly viscid solid. (E) was remethylated (Purdie's reagents), giving a solid (F) (7·0 g.) having $[\alpha]_D^{20°}$ − 60° in methyl alcohol; OMe, 36·1%; equiv. wt., *ca.* 1100. The small amount of methylated pectic acid in (F) was removed by hydrolysing it with dilute alcoholic sodium hydroxide. The excess of alkali was removed by carbon dioxide, and the solution evaporated to dryness. Methylated araban (6 g.) was extracted by acetone, leaving the sodium salt of the pectic acid derivative undissolved. On removal of the acetone, methylated araban (G) was obtained as a cream-coloured powder soluble in acetone, alcohol, chloroform, benzene, and methyl alcohol, but insoluble in water, light petroleum and ether.

The above procedure leads to the isolation of pure methylated araban. In parallel series of experiments much greater amounts of thallium hydroxide were used in the initial stages. In this way some of the araban remained in solution in the thallium hydroxide liquor and was lost, but more complete formation of the thallium derivative of pectic acid took place. It was observed in consequence that increased amounts of the decomposed material (D) were obtained, but the principal feature was that the product at stage (F) of the above scheme contained a very much greater proportion of methylated pectic acid. A typical sample at this stage (yield, 8·0 g. from 25 g. of polysaccharide) had $[\alpha]_D^{20°}$ + 60° in methyl alcohol; OMe, 37%. The araban was removed by hydrolysis with 0·1% methyl-alcoholic hydrogen chloride, which has no action on methylated pectic acid. After neutralisation of the solution with silver carbonate the solvent was evaporated. The product (a sticky solid) was extracted successively with boiling light petroleum and ether, which removed the methylated arabinoses and left methylated pectic acid as a crisp solid having solubilities similar to those of methylated araban, $[\alpha]_D^{20°}$ + 120°; OMe, 33·9%; equiv. wt., 250. This substance was resistant both to further methylation and to hydrolysis by acids. It was sensitive to alkali, undergoing profound decomposition when heated with excess of N-sodium hydroxide. It is not clear from the evidence available whether this material is derived from normal or degraded pectic acid and further investigations are in progress.

*Methylated Araban.*—The material (G) (4·5 g.) was submitted to fractionation by precipitation from chloroform solution by addition of light petroleum. Two fractions were obtained, the first (3·2 g.) being a crisp cream-coloured powder; the second, more soluble portion (1·3 g.) was similar but very slightly sticky, on which account it was discarded. The first fraction had $[\alpha]_D^{20°}$ − 90° in methyl alcohol (*c*, 1·76); $\eta_{sp.}^{20°}/c$ 0·138 in *m*-cresol (*c* in g. per 100 c.c.; since the substance does not possess a straight-chain structure, no calculation of molecular size by Staudinger's method is permissible) (Found: C, 51·8; H, 7·4; OMe, 37·4; $CO_2Me$, nil. Fully methylated araban, $C_7H_{12}O_4$, requires C, 52·5; H, 7·6; OMe, 38·8%. Methylated araban of methoxyl content 37·4% requires C, 52·2; H, 7·6%).

Hydrolysis of methylated araban was carried out by boiling the substance (3·0 g.) for 18 hours, with 1% methyl-alcoholic hydrogen chloride (60 c.c.). The solution was neutralised with silver carbonate and filtered, and the solvent removed by distillation. (It is advisable not to distil off the methyl alcohol under diminished pressure, since trimethyl methylarabofuranoside is volatile under these conditions.) The products of hydrolysis (2·9 g.) were then fractionally distilled, giving:

(i) *2 : 3 : 5-Trimethyl methyl-*l*-arabofuranoside* (0·63 g.), bath temp. 87—90°/0·001 mm.; $n_D^{16.5°}$ 1·4362; $[\alpha]_D^{21°}$ − 60° in water (*c*, 0·6) (Found: OMe, 60·0. $C_9H_{18}O_5$ requires OMe, 60·2%).

(ii) *2 : 3-Dimethyl methyl-*l*-arabinoside* (0·76 g.), bath temp. 115—122°/0·001 mm.; $n_D^{16.5°}$ 1·4522; $[\alpha]_D^{21°}$ + 14° in water (*c*, 0·4) (Found: OMe, 47·7. $C_8H_{16}O_5$ requires OMe, 48·4%).

(iii) *3-Methyl methyl-*l*-arabinoside* (0·64 g.), bath temp. up to 200°/0·001 mm.; $n_D^{16°}$ 1·4710; $[\alpha]_D^{21°}$ + 46° in water (*c*, 0·47) (Found: OMe, 37·6. $C_7H_{14}O_5$ requires OMe, 34·8%. The methoxyl value indicates that this fraction contains a small amount of dimethyl methyl-*l*-arabinoside).

(iv) Residue (0·6 g.). This was a dark tar which could not be further hydrolysed by 3% methyl-alcoholic hydrogen chloride. It probably consisted of the polymerised material formed as by-products when arabinose derivatives are heated with methyl-alcoholic hydrogen chloride. The amounts of fractions (i), (ii), and (iii) indicate a ratio of 1 : 1 : 1 for the trimethyl, dimethyl, and monomethyl portions respectively, the slight deficiency of trimethyl methylarabinoside being readily accounted for by experimental loss due to the high volatility of this fraction (see Carruthers and Hirst, J., 1922, 2304), and that of the third fraction by difficulty in separating it from the non-volatile portion.

2 : 3 : 5-*Trimethyl* l-*Arabinose*.—Fraction (i) (0·57 g.) was hydrolysed by N/10-hydrochloric acid (25 c.c.) at 90° for 8 hours. $[\alpha]_D^{20°}$ − 57° (initial value); − 49° (30 mins.); − 44° (1 hr.); − 26° (2·5 hrs.); − 12° (7 hrs.; constant value). After neutralisation the solution was evaporated to dryness, and the product dissolved in chloroform. On removal of the solvent 2 : 3 : 5-trimethyl *l*-arabinose was obtained as a syrup (0·47 g.), $n_D^{18°}$ 1·4522, $[\alpha]_D^{20°}$ − 14° in water (*c*, 2·4) (Found: OMe, 48·2. Calc. for $C_8H_{16}O_5$: OMe, 48·4%). The trimethyl *l*-arabinose (0·45 g.) in water (2 c.c.) was oxidised by bromine (1 c.c.) at 50° for 1 hour and then at 20° for 12 hours. After removal of the excess of bromine by aeration the solution was neutralised with silver carbonate and filtered immediately, hydrogen sulphide passed through it to remove dissolved silver, and the filtered solution evaporated to dryness. The product (0·41 g.) was distilled, giving 2 : 3 : 5-trimethyl γ-*l*-arabonolactone (0·33 g.), bath temp. 110—115°/0·002 mm.; $n_D^{19°}$ (of superfused solid) 1·4462; m. p. 27—28° (without recrystallisation); $[\alpha]_D^{20°}$ − 44° in water (*c*, 0·8), decreasing after 160 hours to − 30° (mutarotation still not completed) (Found: OMe, 47·8. Calc. for $C_8H_{14}O_5$: OMe, 48·9%. *M*, by titration with *N*/100-sodium hydroxide, 192. Calc., 190). On treatment with methyl-alcoholic ammonia the lactone gave quantitatively the amide of 2 : 3 : 5-trimethyl *l*-arabonic acid, m. p. and mixed m. p. with an authentic specimen, 139°; $[\alpha]_D^{20°}$ + 23° in ethyl alcohol (*c*, 0·3).

2 : 3-*Dimethyl* l-*Arabinose*.—Fraction (ii) (0·61 g.) was hydrolysed by N/10-hydrochloric acid (25 c.c.) for 5 hours at 90°. $[\alpha]_D^{20°}$ + 8° (initial value); + 50° (30 mins.); + 77° (1·5 hrs.); + 89° (2·5 hrs.); + 98° (3·5 hrs.; constant value). The product was isolated in the usual way, giving 2 : 3-*dimethyl* l-*arabinose* (0·55 g.) as a syrup, $n_D^{17°}$ 1·4650, $[\alpha]_D^{20°}$ + 106° (equilibrium value in water; *c*, 2·4) (Found: OMe, 35·7. $C_7H_{14}O_5$ requires OMe, 34·8%). When oxidised by bromine water (for conditions, see above), the sugar (0·53 g.) gave 2 : 3-*dimethyl* γ-l-*arabonolactone* (0·5 g.), obtained after distillation, bath temp. 145—155°/0·003 mm., as a colourless syrup (0·4 g.), $n_D^{17°}$ 1·4605, $[\alpha]_D^{20°}$ − 34° (initial value in water; *c*, 0·7); − 33° (3 hrs.); − 32° (16 hrs.); − 31° (1 day); − 29° (42 hrs.); − 25° (140 hrs.); − 23° (170 hrs.); − 19° (330 hrs., mutarotation still incomplete) (Found: OMe, 35·5; *M*, by titration with N/100-sodium hydroxide, 176. $C_7H_{12}O_5$ requires OMe, 35·2%; *M*, 176). On treatment with methyl-alcoholic ammonia this lactone gave in quantitative yield the *amide* of 2 : 3-dimethyl *l*-arabonic acid, m. p. 160°, $[\alpha]_D^{20°}$ + 17° in water (*c*, 2·2). It was soluble in water, methyl alcohol, ethyl alcohol, less soluble in acetone, ethyl acetate, and nearly insoluble in ether. It was readily recrystallised from ethyl alcohol (Found: C, 43·5; H, 7·7; OMe, 31·7. $C_7H_{15}O_5N$ requires C, 43·4; H, 7·8; OMe, 32·1%). The properties of this amide are in full agreement with those of a sample of 2 : 3-dimethyl *l*-arabonamide prepared from other sources in the Birmingham University laboratories by Haworth and Smith (private communication). When treated with sodium hypochlorite under the conditions given by Weerman (*Rec. Trav. chim.*, 1917, **37**, 16), the above amide gave no trace of sodium *iso*cyanate, as shown by the complete absence of hydrazodicarbonamide after subsequent addition of semicarbazide to the solution.

3-*Methyl* l-*Arabinose*.—Fraction (iii) (0·58 g.) was hydrolysed by N/10-hydrochloric acid for 6 hours at 90°. $[\alpha]_D^{20°}$ + 46° (initial value), rising to + 88° at the end of 3 hours (constant value). After neutralisation with silver carbonate the solution was evaporated to dryness, giving a syrup (0·51 g.) (mainly 3-*methyl* l-*arabinose*), $n_D^{16°}$ 1·4850, $[\alpha]_D^{20°}$ + 96° (equilibrium value in water; *c*, 2·3) (Found: OMe, 21·3 $C_6H_{12}O_5$ requires OMe, 18·9%). (The high methoxyl value indicates the presence of a little dimethyl arabinose.) The sugar (0·49 g.) was oxidised

by bromine water (for conditions, see above), giving the *lactone* as a syrup (0·4 g.), distilling at bath temp. 175°/0·003 mm.; $n_D^{17°}$ 1·4800; $[\alpha]_D^{20°}$ − 36° (initial value in water; *c*, 2·0); − 33° (95 hrs.); − 22° (133 hrs.); − 19° (160 hrs.; mutarotation still incomplete) (Found: OMe, 21·0; *M*, by titration with N/100-sodium hydroxide, 170. $C_6H_{10}O_5$ requires OMe, 19·1%; *M*, 162). When treated with methyl-alcoholic ammonia, the lactone gave the corresponding *amide* as a glassy solid, $[\alpha]_D^{20°}$ + 31° in water (*c*, 1·1) (Found: N, 7·5; OMe, 19·4. $C_6H_{13}O_5N$ requires N, 7·8; OMe, 17·3%). This amide, after treatment with sodium hypochlorite under Weerman's conditions (*loc. cit.*) and subsequent addition of semicarbazide to the solution, gave hydrazodicarbonamide, m. p. and mixed m. p. with an authentic sample, 256°, the yield being identical with that obtained in parallel experiments under the same conditions with *l*-arabonamide.

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THE UNIVERSITY, BRISTOL. [*Received, February 22nd,* 1938.]

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## 105. *Polycyclic Aromatic Hydrocarbons. Part XVII. Completion of the Synthesis of the Twelve Monomethyl-1 : 2-benzanthracenes.*

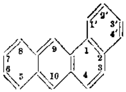
By J. W. COOK and (MRS.) A. M. ROBINSON.

Several monomethyl derivatives of 1 : 2-benzanthracene have very pronounced cancer-producing properties, although the parent hydrocarbon is inactive. As part of an attempt to define the positions of substitution favourable for the development of carcinogenic activity in benzanthracene derivatives a study of these monomethyl compounds has been in progress for some years and the last two members of the series of twelve isomerides have now been synthesised. The condensation of anthracene with succinic anhydride by the Friedel–Crafts reaction has been carried out under such conditions that the pure β-keto-acid (I) is readily isolated, and this has been used for building up the 1 : 2-benzanthracene ring system with the introduction of a methyl group at position 1′ (V). The starting point in the synthesis of 8-methyl-1 : 2-benzanthracene was 3-acetylphenanthrene. This was condensed with ethyl succinate under the influence of sodium ethoxide to give a compound (XIII) having the requisite carbon chain; its reduction product underwent cyclisation in the anticipated manner to give a keto-acid related to 8-methyl-1 : 2-benzanthracene (XV), which was obtained from it in two simple stages. It has been established that a molecular rearrangement accompanies the cyclisation of 2-methyl-1 : 1′-dinaphthyl ketone (VIII) with a fused mixture of aluminium chloride and sodium chloride, for the resulting benzanthrone derivative gave on degradation, not 8-methyl-1 : 2-benzanthraquinone as was hoped, but the 3-methyl isomeride.

TWELVE monomethyl derivatives of 1 : 2-benzanthracene are theoretically possible. Of these, ten have been described already, and we now report the synthesis of the two remaining members of the series with substituents at positions 8 and 1′.* For convenience of reference, the m. p.'s of the whole series of hydrocarbons, with those of their picrates and quinones, are given in the table, in which the corresponding constants of the parent hydrocarbon are also inserted.

Several of these methylbenzanthracenes have carcinogenic properties, in some cases to a high degree. The biological testing of the more recently synthesised members of the series is still at a comparatively early stage and it seems preferable to defer discussion of the contribution which this series makes to the question of the relation between carcinogenic action and molecular structure until the tests are complete.

* Since this paper was written the synthesis of 1′-methyl-1 : 2-benzanthracene by a different type of method has been described by Fieser and Seligman (*J. Amer. Chem. Soc.*, 1938, **60**, 170).




| Position of methyl group. | M. p. of hydrocarbon. | M. p. of picrate. | M. p. of quinone. |
|---|---|---|---|
| — | 160° | 142° | 168° |
| 3 [a] | 155 | 153 | 179 |
| 4 [b] | 125 | 150 | 168 |
| 5 [b] | 158 | 163 | 174 |
| 6 [c] | 151 | 152 | 174 |
| 7 [a] | 182 | — * | 167 |
| 8 | 107 | 161 | 191 |

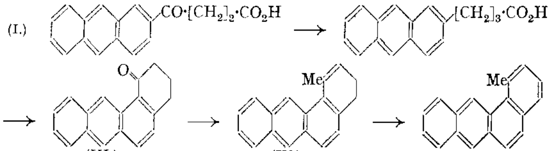
| Position of methyl group. | M. p. of hydrocarbon. | M. p. of picrate. | M. p. of quinone. |
|---|---|---|---|
| 9 [d, e] | 138° | 115° | — |
| 10 [d, f] | 140 | 172 | — |
| 1' | 138 | 119 † | 189° |
| 2' [c] | 150 | 180 | 190 |
| 3' [a] | 160 | 144 | 168 |
| 4' [a] | 194 | 139 | 220 |

[a] Cook, J., 1930, 1087. [b] Cook, J., 1933, 1592 (compare Fieser and Peters, *J. Amer. Chem. Soc.*, 1932, **54**, 3742). [c] Cook, J., 1932, 456. [d] Cook, Robinson, and Goulden, J., 1937, 393. [e] Newman, *J. Amer. Chem. Soc.*, 1937, **59**, 1003. [f] Fieser and Newman, *ibid.*, 1936, **58**, 2376.

* The picrate of 7-methyl-1 : 2-benzanthracene was too readily dissociated for isolation to be possible.

† This is a dipicrate; the other picrates are all monopicrates.

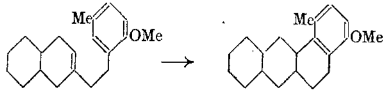
Although the succinic anhydride condensation method has been widely used in recent years for building up an additional condensed ring to polycyclic structures, there appears to be no mention in the literature of the interaction of anthracene with succinic anhydride beyond a statement (Meister Lucius und Brüning, D.R.-P. 376,635) that in nitrobenzene solution this gave a keto-acid of m. p. 160°. Undoubtedly this was a mixture of isomerides. In our hands this reaction has given a mixture of acids, m. p. *ca.* 160°, from which β-2-*anthroylpropionic acid* (I), m. p. 220°, was readily isolated in 18% yield through the medium of its sparingly soluble sodium salt. This was the acid which was required for the synthesis of 1'-*methyl*-1 : 2-*benzanthracene* (V), and the remaining stages of the synthesis, represented by the following scheme, presented no difficulty. The isomeric anthroylpropionic acids present in the crude mixture have not yet been studied.




(I.) (II.) (III.) (IV.) (V.)

Another method by which we had attempted to synthesise 1'-methyl-1 : 2-benzanthracene was an adaptation of the benzanthracene synthesis of Cook and Hewett (J., 1934, 365). For this purpose *trans*-2-decalone was condensed with the Grignard compound of β-4-*methoxy*-m-*tolylethyl chloride* to give a *carbinol*, which was dehydrated to 2-β-(4'-*methoxy*-m-*tolyl*)*ethyl*-$\Delta^{2:3}$-*octalin* (VI). This was cyclised by aluminium chloride to 4'-*methoxy*-1'-*methyldodecahydro*-1 : 2-*benzanthracene* (VII).

(VI.)

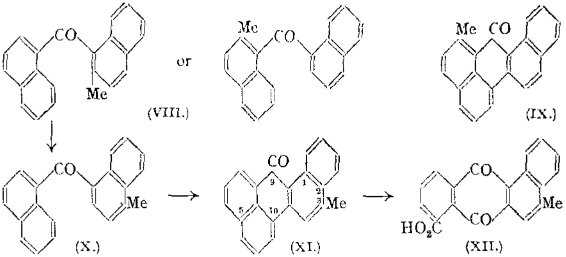



(VII.)

The reason for the presence of the methoxyl group in (VI) was to prevent cyclisation at the *p*-position with respect to the methyl group in the aromatic nucleus, and it was hoped that the methoxyl group could be eliminated after cyclisation, a hope that was encouraged by the knowledge that there are several examples in the literature of the

expulsion of methoxyl groups during selenium dehydrogenation. However, the selenium dehydrogenation of (VII) at 300—310° gave a complex mixture of products, from which the only pure compound isolated, in small yield, was 1 : 2-benzanthracene.

We hoped to obtain 8-methyl-1 : 2-benzanthracene from the methyl-dibenzanthrone (IX) which might conceivably arise by the Scholl *peri*-ring-closure of 2-methyl-1 : 1′-dinaphthyl ketone (VIII). It was subsequently shown, however, that this reaction was accompanied by migration of a methyl group exactly comparable with that observed by Mayer, Fleckenstein, and Günther (*Ber.*, 1930, **63**, 1464) in the analogous case of 1-benzoyl-2-methylnaphthalene, so that the product was 3-*methyl*-1 : 2 : 5 : 10-*dibenz*-9-*anthrone* (XI). The mechanism suggested requires that the same pentacyclic ketone should arise from the action of aluminium chloride on 4-*methyl*-1 : 1′-*dinaphthyl ketone* (X), which is regarded as an intermediate in the conversion of (VIII) into (XI). This was shown to be the case by Dr. de Worms, who was engaged in an investigation of (X) for another purpose.




(VIII.) (IX.) (X.) (XI.) (XII.)

The transformation of (VIII) into (X) is apparently an unusual example of *m*-migration of a methyl group, but we regard it as at least equally probable that the migration is a duplex process consisting of a *p*-migration of the α-naphthoyl group, together with an *o*-migration of methyl to the position which the naphthoyl radical vacates. We are planning experiments to test this hypothesis.

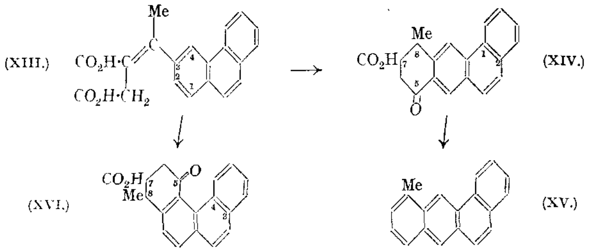
3-*Methyl*-1 : 2-*benzanthraquinone*-5-*carboxylic acid* (XII) was obtained by oxidation of the methyldibenzanthrone (XI) with chromic acid in acetic acid, and was reduced to 3-*methyl*-1 : 2-*benz*-5-*anthroic acid*, which on decarboxylation gave the known 3-methyl-1 : 2-benzanthracene. The identification was completed by comparison of the picrates and quinones, and by crystallographic examination of the two specimens of quinone by Dr. John Iball, who reports as follows :

"The two specimens crystallised from amyl acetate in clusters of needles which had identical appearance. *X*-Ray examination of single crystals of each specimen gave identical photographs and identical unit cell dimensions. The crystals are monoclinic with the *a* axis parallel to the length of the needle. In the case of each specimen the faces developed on the crystals were {011} with a very imperfect {001}. From these facts it can be concluded that both specimens are 3-methyl-1 : 2-benzanthraquinone." Identification of the final hydrocarbon as 3-methyl-1 : 2-benzanthracene provides conclusive proof of the structure (XI) assigned to the methyldibenzanthrone from which it was obtained.

We are indebted to Dr. C. L. Hewett for a suggestion which led to the elaboration of a successful method for the synthesis of 8-methyl-1 : 2-benzanthracene. For this, 3-acetylphenanthrene was condensed with ethyl succinate, and the product hydrolysed to a *methyl-3-phenanthrylitaconic acid* (XIII), which after reduction was cyclised to 5-*keto*-8-*methyl*-5 : 6 : 7 : 8-*tetrahydro*-1 : 2-*benz*-7-*anthroic acid* (XIV). Clemmensen reduction of this keto-acid, followed by dehydrogenation–decarboxylation with platinum-black, gave the desired 8-*methyl*-1 : 2-*benzanthracene* (XV).

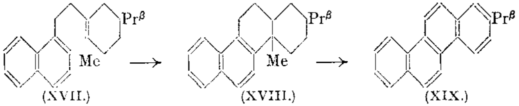
A minor product of the cyclisation of the saturated acid obtained by reduction of (XIII) was 5-*keto*-8-*methyl*-5 : 6 : 7 : 8-*tetrahydro*-3 : 4-*benz*-7-*phenanthroic acid* (XVI), in

which the carbonyl group was inert towards semicarbazide. Ring-closure of a derivative c γ-3-phenanthrylbutyric acid at position 4 has not hitherto been observed, althoug




Bachmann and Kloetzel (*J. Amer. Chem. Soc.*, 1937, **59**, 2207) have shown that cyclisation of β-3-phenanthrylpropionic acid takes place almost exclusively at position 4. These relationships furnish additional illustration of the difficulty of formation of the ring system of 3 : 4-benzphenanthrene (compare Hewett, J., 1936, 596).

The present communication provides a convenient opportunity to record the synthesis of 4-iso*propylchrysene* (XIX), the carcinogenic inactivity of which has been reported elsewhere (Bachman *et al.*, *Proc. Roy. Soc.*, 1937, *B*, **123**, 363). This was obtained by selenium dehydrogenation of the *methyl*iso*propyloctahydrochrysene* (XVIII) resulting from cyclisation of 2-*methyl*-1-(β-1'-*naphthylethyl*)-5-iso*propyl*-$\Delta^1$-cyclo*hexene* (XVII), which in its turn was prepared by dehydration of the crude carbinol resulting from interaction of β-1-naphthylethylmagnesium chloride with tetrahydrocarvone.




An attempt to prepare a methyl*iso*propylchrysene from tetrahydrocarvone was frustrated by the failure of the potassio-compound of *ethyl* 6-*methyl*-3-iso*propyl*cyclo*hexanone*-2-*carboxylate* to condense with β-1-naphthylethyl bromide.

## Experimental.

### 1'-*Methyl*-1 : 2-*benzanthracene*.

β-2-*Anthroylpropionic Acid* (I).—Succinic anhydride (100 g.) was dissolved in nitrobenzene (1 l.) at 60—70°, the solution cooled to 20° and finely powdered anhydrous aluminium chloride (133 g.) gradually added. The mechanically stirred mixture was cooled to 5°, treated slowly with powdered anthracene (178 g.), and kept at 5—10° for 72 hours. The product was diluted with dry benzene (500 c.c.) and the precipitate was collected. This consisted mainly of anthracene (70 g.) together with a little of the acidic condensation product (5 g.), which was extracted with dilute sodium carbonate solution. The benzene and nitrobenzene were removed from the filtrate by steam distillation; the residue was collected after cooling, dissolved in dilute sodium carbonate solution (1 l.), and filtered hot. The sodium salt which crystallised on cooling was collected, and the free acid liberated (35 g.). β-2-*Anthroylpropionic acid* (I) crystallised from ethyl acetate in yellow prismatic needles, m. p. 220—221° (Found : C, 77·7; H, 5·1. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·1%). The *methyl* ester formed pale yellow leaflets (from alcohol), m. p. 144·5—145·5° (Found : C, 78·0; H, 5·5. $C_{19}H_{16}O_3$ requires C, 78·05; H, 5·5%). The orientation of this keto-acid was shown by its oxidation to anthraquinone-2-carboxylic acid. This was carried out in two stages, the first with sodium dichromate in boiling glacial acetic acid, and the second with dilute alkaline permanganate solution. The product crystallised from concentrated

nitric acid in soft yellowish needles, m. p. 287—288°, not depressed by authentic anthraquinone-2-carboxylic acid, but depressed to 250° by anthraquinone-1-carboxylic acid.

*γ-2-Anthrylbutyric Acid* (II).—A mixture of β-2-anthroylpropionic acid (10 g.), glacial acetic acid (100 c.c.), concentrated hydrochloric acid (100 c.c.), toluene (20 c.c.), and amalgamated zinc (30 g.) was boiled under reflux for 20 hours, further portions of concentrated hydrochloric acid (20 c.c.) being added hourly during the first 8 hours. The toluene was removed in steam, the residual solid collected and purified through its sparingly soluble sodium salt, and the regenerated acid twice recrystallised from glacial acetic acid (yield, 6·6 g.) and then from benzene. *γ-2-Anthrylbutyric acid* (II) formed colourless rectangular plates, m. p. 194—195° (Found: C, 81·9; H, 6·2. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%).

*1′-Keto-1′ : 2′ : 3′ : 4′-tetrahydro-1 : 2-benzanthracene* (III).—(a) This was obtained in 65% yield when γ-2-anthrylbutyric acid was heated at 100° for 1½ hours with anhydrous stannic chloride (1·5 c.c. per g.). The product, freed from stannic chloride by repeated extraction with concentrated hydrochloric acid, was twice recrystallised from alcohol, sublimed at 0·2 mm., and finally crystallised from alcohol. *1′-Keto-1′ : 2′ : 3′ : 4′-tetrahydro-1 : 2-benzanthracene* (III) formed pale yellow plates, m. p. 114—114·5° (Found: C, 87·9; H, 5·75. $C_{18}H_{14}O$ requires C, 87·8; H, 5·7%).

(b) Phosphorus pentachloride (4·5 g.) was added to a suspension of γ-2-anthrylbutyric acid (5 g.) in benzene (50 c.c.), and the solution heated to boiling, and then cooled to 5°, with stirring. Anhydrous aluminium chloride (6·5 g.) was then gradually added, and stirring continued for 6 hours at room temperature. The product was decomposed with ice and hydrochloric acid, the benzene removed in steam, and the ketone (III) freed from unchanged acid (0·7 g.) and recrystallised from alcohol. The yield was 3 g.

*1′-Methyl-3′ : 4′-dihydro-1 : 2-benzanthracene* (IV).—The aforesaid ketone (4 g.) was slowly added to a Grignard solution prepared from methyl iodide (8·5 g.) and magnesium turnings (1·4 g.) in anhydrous ether (100 c.c.). The mixture was boiled for 3 hours and decomposed with ice and ammonium chloride, and the resulting crude carbinol was dehydrated by ½ hour's boiling in alcoholic solution (30 c.c.) with picric acid (4 g.). The *picrate* of 1′-methyl-3′ : 4′-dihydro-1 : 2-benzanthracene (7 g.), which crystallised on cooling, formed purplish-black clusters of needles, m. p. 120—121° (Found: C, 63·5; H, 4·2. $C_{19}H_{16},C_6H_3O_7N_3$ requires C, 63·4; H, 4·05%). *1′-Methyl-3′ : 4′-dihydro-1 : 2-benzanthracene*, obtained from this picrate by shaking with benzene and dilute sodium carbonate solution, was distilled at 0·001 mm., and twice recrystallised from ligroin; it then formed pale yellow, laminated needles, m. p. 74—75° (Found: C, 93·1; H, 6·4. $C_{19}H_{16}$ requires C, 93·4; H, 6·6%).

*1′-Methyl-1 : 2-benzanthracene* (V).—The crude dihydro-compound (3 g.) was rapidly dehydrogenated when heated at 250° with platinum-black (0·3 g.) in an atmosphere of carbon dioxide. After an hour at this temperature the product was crystallised from a little benzene, sublimed at 0·1 mm., and recrystallised from ethyl acetate. *1′-Methyl-1 : 2-benzanthracene* (V) formed almost colourless leaflets, m. p. 137·5—138·5°, which gave the characteristic 1 : 2-benzanthracene colour reaction with concentrated sulphuric acid (Found: C, 94·0; H, 6·0. $C_{19}H_{14}$ requires C, 94·2; H, 5·8%). The m. p. was not changed after regeneration from the purified *dipicrate*, which formed scarlet needles (from benzene), m. p. 119° (Found: C, 53·4; H, 3·1. $C_{19}H_{14},2C_6H_3O_7N_3$ requires C, 53·1; H, 2·9%). The crude quinone obtained by oxidation of the hydrocarbon with sodium dichromate in boiling acetic acid was purified by reduction with zinc dust and boiling dilute sodium hydroxide, followed by aerial oxidation of the filtered blood-red solution. The precipitate was collected, dried, and sublimed at 0·05 mm., and the sublimate was recrystallised from ethyl acetate. *1′-Methyl-1 : 2-benzanthraquinone* formed orange needles, m. p. 188·5—189·5° (Found: C, 83·8; H, 4·5. $C_{19}H_{12}O_2$ requires C, 83·8; H, 4·4%).

*β-4-Methoxy-m-tolylethyl Chloride.*—Ethylene oxide (25 g.) was added slowly to a well-cooled Grignard solution prepared from 3-bromo-4-methoxytoluene (86 g.) (Schall and Dralle, *Ber.*, 1884, **17**, 2531; compare Anderson, *J. Biol. Chem.*, 1916, **26**, 393) and magnesium turnings (10·3 g.) in dry ether (400 c.c.). After the mixture had been kept overnight at room temperature, the ether was removed by distillation, and the residue was heated on a boiling water-bath for 1½ hours and then decomposed with ice and hydrochloric acid. The resulting *β-4-methoxy-m-tolylethyl alcohol* (b. p. 150—160°/18 mm.; 37 g.) crystallised from ligroin in colourless prismatic needles, m. p. 45—46° (Found: C, 72·4; H, 8·7. $C_{10}H_{14}O_2$ requires C, 72·2; H, 8·5%). *β-4-Methoxy-m-tolylethyl chloride*, obtained in the usual way by the action of thionyl chloride on the alcohol, in dimethylaniline, formed a colourless liquid, b. p. 126—127°/12 mm. (Found: C, 64·85; H, 7·2. $C_{10}H_{13}OCl$ requires C, 65·0; H, 7·1%).

*2-β-(4′-Methoxy-m-tolyl)ethyl-$\Delta^{2:3}$-octalin* (VI).—*trans*-2-Decalone (18·5 g.) was added to an

ice-cold Grignard solution prepared from the foregoing chloride (22 g.) and magnesium turnings (2 g.) in ether (120 c.c.) and anisole (40 c.c.). After ½ hour at 0° the mixture was boiled for 1½ hours and decomposed with ice and ammonium chloride, and the tertiary carbinol isolated by distillation. It formed a glassy solid, b. p. 175—185°/0·3 mm., and gave a 3 : *5-dinitrobenzoate*, m. p. 117—117·5° (from alcohol) (Found: C, 65·3; H, 6·6. $C_{27}H_{32}O_7N_2$ requires C, 65·3; H, 6·5%). 2-β-(*4'-Methoxy*-m-*tolyl)ethyl*-$\Delta^{2 \cdot 3}$-*octalin* (VI), obtained from the carbinol by heating with potassium hydrogen sulphate (1½ parts) at 170—180° for 2 hours, formed a colourless liquid, b. p. 178—180°/0·5 mm., after distillation over sodium (Found: C, 84·0; H, 10·15. $C_{20}H_{28}O$ requires C, 84·45; H, 9·9%).

*4'-Methoxy-1'-methyldodecahydro-1 : 2-benzanthracene* (VII).—A mixture of the octalin (VI) (10 g.), carbon disulphide (100 c.c.), and aluminium chloride (14 g.) was kept at 0° for 4 hours and then at room temperature overnight. The solution was decanted, washed, and fractionated. The fraction (7 g.), b. p. 175—185°/0·5 mm., solidified when triturated with methyl alcohol, and the resulting *4'-methoxy-1'-methyldodecahydro-1 : 2-benzanthracene* (VII) (4·5 g.) crystallised from methyl alcohol in long colourless needles, m. p. 80·5—81° (Found: C, 84·1; H, 10·1. $C_{20}H_{28}O$ requires C, 84·45; H, 9·9%).

### *3-Methyl-1 : 2-benzanthracene from 2-Methyl-1 : 1'-dinaphthyl Ketone.*

*3-Methyl-1 : 2 : 5 : 10-dibenz-9-anthrone* (XI).—(a) An intimate mixture of 2-methyl-1 : 1'-dinaphthyl ketone (Clar, *Ber.*, 1929, **62**, 350) (35 g.), anhydrous aluminium chloride (140 g.), and sodium chloride (35 g.) was stirred mechanically in a bath gradually heated to 110°. At this temperature the mass began to liquefy and a vigorous reaction ensued. The temperature was then maintained at 80—90° for 1½ hours, stirring being continued, and the product was poured on ice and hydrochloric acid. After 12 hours the solid was collected and recrystallised from glacial acetic acid. The resulting *3-methyl-1 : 2 : 5 : 10-dibenz-9-anthrone* (XI) (18 g.) was almost pure; a sample for analysis, sublimed at 160—200°/0·05 mm. and crystallised from glacial acetic acid, formed fine golden-yellow needles, m. p. 221—222° (Found: C, 89·6; H, 5·05. $C_{22}H_{14}O$ requires C, 89·8; H, 4·8%).

(b) * Finely powdered aluminium chloride (20 g.) was added during ½ hour to an ice-cold mixture of 1-methylnaphthalene (20 g.), 1-naphthoyl chloride (23 g.), and carbon disuphide (65 c.c.). After 5½ hours with occasional shaking, the product was decomposed with ice and hydrochloric acid, the carbon disulphide and the excess of methylnaphthalene removed in steam, naphthoic acid extracted with dilute sodium carbonate solution, and the residual crude ketone distilled (b. p. 275—280°/0·6 mm.). The distillate was recrystallised from glacial acetic acid and then from alcohol. *4-Methyl-1 : 1'-dinaphthyl ketone* (X) formed colourless octahedra, m. p. 100—101·5° (Found: C, 88·9; H, 5·4. $C_{22}H_{16}O$ requires C, 89·15; H, 5·4%), and its *picrate* crystallised from alcohol in yellow rosettes, m. p. 86—87·5° (Found: C, 63·95; H, 3·85. $C_{22}H_{16}O,C_6H_3O_7N_3$ requires C, 64·0; H, 3·65%). The constitution assigned to this ketone (X) was confirmed by its preparation from 1-naphthonitrile and the Grignard compound of 4-bromo-1-methylnaphthalene, the structure of which rests on fairly secure foundation (see Mayer and Sieglitz, *Ber.*, 1922, **55**, 1835).

Cyclisation of 4-methyl-1 : 1'-dinaphthyl ketone to 3-methyl-1 : 2 : 5 : 10-dibenz-9-anthrone (XI) by an aluminium chloride–sodium chloride melt was effected as described under (a). The product had m. p. 221—222°, not depressed by the compound prepared from 2-methyl-1 : 1'-dinaphthyl ketone (VIII).

*3-Methyl-1 : 2-benzanthraquinone-5-carboxylic Acid* (XII).—A solution of chromic anhydride (35 g.) in 80% acetic acid (70 c.c.) was added dropwise during an hour to a boiling suspension of 3-methyl-1 : 2 : 5 : 10-dibenz-9-anthrone (9·4 g.) in glacial acetic acid (200 c.c.). Boiling was continued for another hour, and the green solution was concentrated in a vacuum on the water-bath until no more acetic acid distilled. The residue was extracted with water, treated with excess of sodium carbonate, boiled, and filtered hot. The chromium hydroxide sludge was extracted three times with a large volume of boiling dilute sodium carbonate solution. The combined alkaline liquors were acidified and the precipitated acid was collected and dried (yield, 5·35 g.). Purification was effected by crystallisation of the sparingly soluble sodium salt from water. *3-Methyl-1 : 2-benzanthraquinone-5-carboxylic acid* (XII) crystallised from a large volume of glacial acetic acid in small orange needles, m. p. 305—306° (Found: C, 75·8; H, 3·9. $C_{20}H_{12}O_4$ requires, C, 75·9; H, 3·8%).

*3-Methyl-1 : 2-benz-5-anthroic Acid.*—A solution of stannous chloride (13·5 g.) in concentrated

* These experiments were carried out by Dr. C. G. M. de Worms.

hydrochloric acid (40 c.c.) was added to a suspension of the quinone-acid (XII) (3·25 g.) in glacial acetic acid (500 c.c.), and the mixture boiled for an hour. After cooling, the crystalline anthranol acid was collected and reduced further by 9 hours' boiling with zinc dust (20 g.) in N-sodium hydroxide (300 c.c.). The cooled suspension of sodium salt and excess of zinc was filtered off, and the solid digested with hydrochloric acid until the zinc was dissolved. The residual 3-*methyl*-1 : 2-*benz*-5-*anthroic acid* crystallised from a large volume of glacial acetic acid as a yellow crystalline powder, m. p. 320—322° (decomp.) (Found: C, 83·3; H, 5·0. $C_{20}H_{14}O_2$ requires C, 83·9; H, 4·9%). The *methyl* ester formed lemon-yellow irregular plates (from ethyl acetate), m. p. 170—171° (Found: C, 83·5; H, 5·6. $C_{21}H_{16}O_2$ requires C, 84·0; H, 5·4%).

3-*Methyl*-1 : 2-*benzanthracene*.—This was obtained by decarboxylation of 3-methyl-1 : 2-benz-5-anthroic acid (1·2 g.) with copper-bronze (0·5 g.) in boiling quinoline (25 c.c.) (2 hours). The hydrocarbon was sublimed at 160°/0·1 mm. and recrystallised from benzene-alcohol, forming colourless plates, m. p. 155° (Found: C, 94·2; H, 5·9. Calc.: C, 94·2; H, 5·8%); it gave a *picrate*, m. p. 153° (from benzene) (Found: C, 63·7; H, 3·8. $C_{19}H_{14},C_6H_3O_7N_3$ requires C, 63·7; H, 3·6%). The quinone obtained by oxidation had m. p. 177° (Found: C, 83·6; H, 4·5. Calc.: C, 83·8; H, 4·4%). These three compounds gave no depression of m. p. when mixed with authentic specimens prepared from phthalic anhydride and 1-methylnaphthalene (Scholl and Tritsch, *Monatsh.*, 1911, **32**, 997; Cook, J., 1930, 1087). The constitution of the intermediate 4-methyl-*o*-1-naphthoylbenzoic acid was confirmed by the preparation of the same acid, m. p. 169°, from phthalic anhydride and 4-methyl-1-naphthylmagnesium bromide, the technique of Weizmann, Bergmann, and Bergmann (J., 1935, 1367) being used.

8-*Methyl*-1 : 2-*benzanthracene*.

*Methyl*-3-*phenanthrylitaconic Acid* (XIII).—Absolute ethyl alcohol (15·4 g.) was added to fine sodium wire (7·7 g.) covered with anhydrous ether, and the suspension kept for 24 hours. Most of the ether was distilled off, the temperature raised to 60—70°, and a warm ethereal solution of 3-acetylphenanthrene (Mosettig and van de Kamp, *J. Amer. Chem. Soc.*, 1930, **52**, 3704) (37 g.) and ethyl succinate (29·6 g.) slowly added. A vigorous reaction set in. The ether and alcohol were removed by distillation, water added to the residue, and insoluble material extracted with ether. The aqueous solution was refluxed for 6 hours after addition of sodium hydroxide (20 g.). It was then cooled and the sodium salt which crystallised was collected, dissolved in water, and acidified. The precipitate was recrystallised from acetic acid and gave 3 g. of acid, m. p. 191—192°. The alkaline liquors were acidified and extracted with ether. The ether was removed from the extract, and the residue triturated with benzene. The undissolved residue was recrystallised from acetic acid and gave another 22 g. of the same acid, m. p. 191°. For analysis, *methyl*-3-*phenanthrylitaconic acid* (XIII) was purified through its anhydride and crystallised from ethyl acetate; it then formed colourless prisms, m. p. 192—193° (Found: C, 75·0; H, 5·0. $C_{20}H_{16}O_4$ requires C, 75·0; H, 5·0%).

The *anhydride*, obtained by boiling with acetyl chloride, formed a microcrystalline colourless powder (from chloroform), m. p. 203° (Found: C, 79·0; H, 4·8. $C_{20}H_{14}O_3$ requires C, 79·45; H, 4·7%).

α-(α'-3-*Phenanthrylethyl*)*succinic Acid*.—A solution of the unsaturated acid (XIII) (17 g.) in water (1700 c.c.) and sodium hydroxide (5·1 g.) was heated at 60—70° for 120 hours, during which five portions of 2·5% sodium amalgam (170 g.) were added. The solution was cooled and the sodium salt which crystallised (13·5 g.) was collected. The acid obtained from this was combined with a little more obtained from the liquors and recrystallised from aqueous acetic acid, yielding 13·5 g. of saturated acid, m. p. 178—179°. For analysis, a specimen was recrystallised from ethyl acetate and then aqueous methyl alcohol. α-(α'-3-*Phenanthrylethyl*)*succinic acid* formed colourless leaflets, m. p. 183° (Found: C, 74·3; H, 5·7. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6%).

The *anhydride* was obtained by refluxing a suspension of this acid (5 g.) in acetyl chloride (30 c.c.) for 4 hours. The cooled solution was filtered, the acetyl chloride removed under reduced pressure, and the residue recrystallised from benzene-light petroleum; it then had m. p. 142—143°. A specimen of this anhydride crystallised from *cyclo*hexane in colourless needles, m. p. 145° (Found: C, 78·9; H, 5·3. $C_{20}H_{16}O_3$ requires C, 78·9; H, 5·3%).

5-*Keto*-8-*methyl*-5 : 6 : 7 : 8-*tetrahydro*-1 : 2-*benz*-7-*anthroic Acid* (XIV).—A solution of α-(α'-3-phenanthrylethyl)succinic anhydride (10 g.) in nitrobenzene (50 c.c.) was added dropwise during ½ hour to an ice-cold solution of anhydrous aluminium chloride (10 g.) in nitrobenzene (50 c.c.). The blood-red solution was kept at 0° for 20 hours and then decomposed with ice and hydrochloric acid and freed from nitrobenzene by steam distillation. The residual solid was

collected and dissolved in hot dilute sodium carbonate solution, and the filtered solution cooled. The sodium salt which crystallised was collected; it gave the desired keto-acid (XIV) (6 g.), which crystallised from aqueous acetic acid in colourless plates, m. p. 214—215°. For analysis, a specimen was purified through its *semicarbazone*, which formed colourless silky needles, m. p. 275° (decomp.), too sparingly soluble to be recrystallised (Found: N, 11·15. $C_{21}H_{19}O_3N_3$ requires N, 11·6%). This semicarbazone was largely unattacked after being heated at 180—190° for 17 hours with alcoholic sodium ethoxide. *5-Keto-8-methyl-5 : 6 : 7 : 8-tetrahydro-1 : 2-benz-7-anthroic acid* (XIV), obtained by hydrolysis of the semicarbazone, was sublimed at 200°/0·01 mm. and recrystallised from benzene, in which it was very sparingly soluble. It formed a colourless microcrystalline powder, m. p. 214—215° (Found: C, 78·6; H, 5·4. $C_{20}H_{16}O_3$ requires C, 78·9; H, 5·3%).

The alkaline mother-liquors, from which the sparingly soluble sodium salt of this acid had been separated, were acidified and the precipitate was recrystallised from aqueous acetic acid. The product (1·7 g.) was sublimed at 210°/0·01 mm., and the sublimate was treated with semicarbazide in boiling aqueous alcoholic solution. A small amount of sparingly soluble semicarbazone was separated; the bulk of the material had not reacted with semicarbazide and was recrystallised twice from alcohol and then from toluene. This keto-acid (yield, 0·5 g.), which was much more soluble than its isomeride (XIV), was undoubtedly *5-keto-8-methyl-5 : 6 : 7 : 8-tetrahydro-3 : 4-benz-7-phenanthroic acid* (XVI), formed by cyclisation at the alternative position 4 of the phenanthrene ring system. It formed colourless prismatic needles, m. p. 177—178°, and its failure to react with semicarbazide is readily explicable on stereochemical grounds (Found: C, 79·1; H, 5·45. $C_{20}H_{16}O_3$ requires C, 78·9; H, 5·3%).

The keto-acid (XIV) was also obtained, in less satisfactory yield, by cyclisation of the succinic anhydride derivative with stannic chloride at 100°. The sample prepared by this method had m. p. 217°.

*8-Methyl-5 : 6 : 7 : 8-tetrahydro-1 : 2-benz-7-anthroic Acid.*—This was obtained by Clemmensen reduction of the keto-acid (XIV). To this end the keto-acid (5 g.) was boiled under reflux for 24 hours with acetic acid (15 c.c.), water (25 c.c.), concentrated hydrochloric acid (30 c.c.), toluene (10 c.c.), and amalgamated granulated zinc (15 g.). At the end of each of the first 5 hours additional concentrated hydrochloric acid (10 c.c.) was added. Examination of the product indicated that it probably still contained some of the sparingly soluble keto-acid, and the whole was submitted anew to the above treatment, boiling being prolonged for 48 hours. The product was isolated, and esterified with methyl-alcoholic hydrogen chloride, and the methyl ester distilled at 0·1 mm. from a bath gradually heated from 220° to 280°. The viscous distillate (3·5 g.) was hydrolysed with boiling aqueous alcoholic alkali, and the acid recrystallised from aqueous acetic acid. *8-Methyl-5 : 6 : 7 : 8-tetrahydro-1 : 2-benz-7-anthroic acid* (2·9 g.) formed colourless needles, m. p. 215—217°, unaltered by recrystallisation from toluene and then benzene (Found: C, 82·7; H, 6·3. $C_{20}H_{18}O_2$ requires C, 82·7; H, 6·3%).

*8-Methyl-1 : 2-benzanthracene.*—The foregoing acid (2·8 g.) was heated with platinum-black (0·5 g.) at 300—310° for 5 hours in an atmosphere of carbon dioxide. The product was extracted with ether and washed with dilute sodium carbonate solution, which removed 0·6 g. of unchanged acid. The neutral fraction from the ethereal extract was distilled from an air-bath at 145—155°/0·02 mm. The distillate was recrystallised from alcohol, and gave 1·45 g. of crude hydrocarbon, m. p. 102—114°. This was purified through its *s-trinitrobenzene complex*, which crystallised from alcohol in long scarlet needles, m. p. 164—165° (Found: C, 66·2; H, 4·1. $C_{19}H_{14},C_6H_3O_6N_3$ requires C, 65·9; H, 3·8%). To recover the hydrocarbon, a boiling alcoholic suspension of this complex was treated with a solution of stannous chloride in concentrated hydrochloric acid, boiling being continued for a few minutes. The resulting 8-methyl-1 : 2-benzanthracene (m. p. 107—109°) was further purified by crystallisation of its picrate from benzene. This *picrate*, recrystallised for analysis from alcohol, formed reddish-brown needles, m. p. 161—162° (Found: C, 63·8; H, 3·8. $C_{19}H_{14},C_6H_3O_7N_3$ requires C, 63·7; H, 3·6%). The hydrocarbon regenerated from the picrate was sublimed at 150°/0·01 mm., and then recrystallised from alcohol. *8-Methyl-1 : 2-benzanthracene* formed colourless leaflets, m. p. 107°, and gave the series of colours in concentrated sulphuric acid characteristic of the benzanthracene hydrocarbons (Found: C, 94·2; H, 5·8. $C_{19}H_{14}$ requires C, 94·2; H, 5·8%).

*8-Methyl-1 : 2-benzanthraquinone* was obtained by oxidation of the hydrocarbon with sodium dichromate (2 parts) in glacial acetic acid, and was purified as described for the 1′-methyl compound (p. 509). It formed long canary-yellow needles (from ethyl acetate), m. p. 191—192°, and gave large depressions of m. p. when mixed with 1′-methyl- or 2′-methyl-1 : 2-benzanthraquinone (Found: C, 83·7; H, 4·5. $C_{19}H_{12}O_2$ requires C, 83·8; H, 4·4%).

4-iso*Propylchrysene.*

*2-Methyl-1-(β-1'-naphthylethyl)-5-*iso*propyl-Δ¹-*cyclo*hexene* (XVII).—Tetrahydrocarvone (31 g.)* was added slowly to an ice-cold Grignard solution prepared from β-1-naphthylethyl chloride (47 g.), magnesium turnings (6 g.), and anhydrous ether (125 c.c.). The mixture was then boiled for 24 hours and decomposed with ice and ammonium chloride, the crude distilled carbinol (b. p. 217—218°/0·8 mm.; 10 g.) dehydrated with potassium hydrogen sulphate at 160—180°, and the product purified by crystallisation from alcohol of its easily soluble picrate. *2-Methyl-1-(β-1'-naphthylethyl)-5-*iso*propyl-Δ¹-*cyclo*hexene* (XVII) formed a colourless viscous liquid, b. p. 160—165°/0·15 mm. (Found: C, 90·4; H, 9·65. $C_{22}H_{28}$ requires C, 90·35; H, 9·65%).

4-iso*Propylchrysene* (XIX).—Cyclisation of the unsaturated hydrocarbon (XVII) (5 g.) with aluminium chloride (6 g.) in carbon disulphide (30 c.c.) at 0° was complete in 24 hours. The distilled product (b. p. 195°/0·2 mm.) gave crystals of *methyl*iso*propyloctahydrochrysene* (XVIII), which formed colourless rectangular plates, m. p. 108° after recrystallisation from alcohol (Found: C, 89·8; H, 9·7. $C_{22}H_{28}$ requires C, 90·35; H, 9·65%). This was dehydrogenated by selenium at 320° (24 hours) to 4-iso*propylchrysene* (XIX), which crystallised from alcohol in colourless plates, m. p. 227° (Found: C, 93·0; H, 6·75. $C_{21}H_{18}$ requires C, 93·3; H, 6·7%), and gave a 2 : *7-dinitroanthraquinone complex*, m. p. 241—242° (Found: C. 74·2; H, 4·3. $C_{21}H_{18},C_{14}H_6O_6N_2$ requires C, 74·5; H, 4·3%).

*Ethyl 6-Methyl-3-*iso*propyl*cyclo*hexanone-2-carboxylate.*—Tetrahydrocarvone was converted by the procedure of Simonsen, Bradfield, and Jones (J., 1935, 315) into α-methyl-δ-*iso*propylpimelic acid and this was esterified with alcoholic hydrogen chloride. The *ethyl* ester formed a colourless liquid, b. p. 110°/0·5 mm. (Found: C, 66·0; H, 10·45. $C_{15}H_{28}O_4$ requires C, 66·1; H, 10·4%). The Dieckmann cyclisation of this ester (12 g.) was effected by heating it for 6 hours at 120—130° with sodium (1·7 g.) in dry toluene (30 c.c.) (compare Cornubert and Borrel, *Bull. Soc. chim.*, 1930, **47**, 301). After fractionation, the resulting *ethyl 6-methyl-3-*iso*propyl*cyclo*hexanone-2-carboxylate* formed a colourless liquid, b. p. 100°/0·2 mm. (Found: C, 69·5; H, 10·2. $C_{13}H_{22}O_3$ requires C, 69·0; H, 9·8%), and gave no condensation product when its potassio-compound was heated under reflux in benzene solution for 8 days with β-1-naphthylethyl bromide.

We are indebted to the International Cancer Research Foundation for a grant which has enabled one of us (A. M. R.) to participitate in this work, and to the British Empire Cancer Campaign for grants which have supported this investigation.

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## 106. *The Action of Alkali on Rotenone and Related Substances.*

By R. S. CAHN, R. F. PHIPERS, and J. J. BOAM.

The precursor of toxicarol in *Derris* extract is purified and shown to be the *l*-form of the known toxicarol.

Very mild alkali, *e.g.*, potassium carbonate or a trace of alkali hydroxide in acetone, alkali acetate in alcohol, alkali hydroxide in benzene–methyl alcohol, or "activated" alumina in non-hydroxylic solvents, racemises the two central tertiary carbon atoms of rotenone, toxicarol, and related substances by enolisation, followed by fission of the dihydropyranone ring. The same conditions lead to equilibration of toxicarol with a structural isomeride, and proof of the structure of this isomeride also proves the mechanism postulated for the racemisation. Changes in rotation and absorption spectra in the presence of alkali indicate that enolisation is more facile in the toxicarol than in the rotenone series. In all cases one form of ring-junction is greatly favoured.

THE "resin" or "extract" removed by organic solvents such as ether, benzene, etc., from the roots of *Derris elliptica* has long been known to contain rotenone. From so-called "Sumatra-type" *Derris* roots Cahn and Boam (*J. Soc. Chem. Ind.*, 1935, **54**, 42T) isolated sumatrol. By freeing the extract as far as possible from rotenone and treating

* We are indebted to Messrs. Howards and Sons, Ltd., for the preparation of this ketone.

the residual gum with alkali, three substances have been isolated, namely, toxicarol, deguelin, and tephrosin [Clark, *J. Amer. Chem. Soc.*, (*a*) 1930, **52**, 2461; (*b*) 1931, **53**, 313; (*c*) 1931, **53**, 729. Haller and LaForge, (*a*) *ibid.*, 1934, **56**, 2415. Cahn and Boam, *loc. cit.* Buckley, *J. Soc. Chem. Ind.*, 1936, **55**, 285T. Back-reference to papers by Clark, Haller, LaForge, and their collaborators will be made by the letters *a*, *b*, etc. Papers by Haller or LaForge and their collaborators form one series]. Buckley (*loc. cit.*) reports a fourth substance, m. p. 183°, obtained by treatment with alkali, but we have never encountered it and consider its individuality as yet insufficiently established. It is now generally recognised that toxicarol, deguelin, and tephrosin do not exist as such in the extract; tephrosin is formed by oxidation of deguelin during its isolation, and deguelin and toxicarol result from some change in the original components caused by the alkali used for their isolation. Rotenone and sumatrol are lævorotatory. Toxicarol, deguelin, and tephrosin, as isolated, are optically inactive. Haller and LaForge's work made it probable, but not certain, that deguelin existed in the extract at least partly as the *l*-isomeride.

Failing, as did also other workers, to isolate other ingredients from the extract without the use of alkali, we investigated the effect of alkali on rotenone and derived substances of known structure in the hope, ultimately realised, that knowledge of this action would throw light on the nature of the deguelin and toxicarol precursors. In this paper we describe (*A*) the action of alkali on rotenone and similar substances and (*B*) the action of alkali on toxicarol.

When this work had been completed, Tattersfield and Martin (*Ann. Appl. Biol.*, 1936, **23**, 899; *J. Soc. Chem. Ind.*, 1937, **56**, 77T, 88T) isolated from *Derris* a substance, m. p. 99°, $[\alpha]_D$ −70° in benzene, which yielded inactive toxicarol when treated with alkali and was correctly considered by them to be the precursor, or a mixture of precursors, of toxicarol. In section (*C*) we show that their product was not quite pure and we establish its constitution.

The bearing of our results on the nature of the components of *Derris* extract and the quantitative determination of 90% of its total ingredients are discussed by us elsewhere (*J. Soc. Chem. Ind.*, in the press).

Unusual difficulties are caused in this field by dimorphism, variability of melting points, and, occasionally though not often, absence of mixed melting point depressions. It is thus essential that claims to individuality or identity should be thoroughly established; preparation of a series of derivatives, optical rotation (values in the series are large and differ widely), crystallo-optical data, and, occasionally, absorption spectra are suitable for this purpose. We have been at pains in our work to indicate clearly the means of identification in all cases in which it seemed to us at all doubtful.

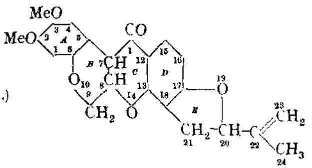
### A. *Action of Alkali on Rotenone and Derived Substances.*

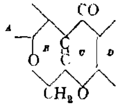
Tattersfield and Martin (*loc. cit.*) showed that addition of large amounts of methyl-alcoholic potassium hydroxide to rotenone in benzene caused a gradual fall in optical rotation, the rate depending largely on the amount of alcohol added. At the time of this publication we had already carried out rather similar experiments, in which, however, we used other solvents and very much milder alkaline conditions, and we had also fully elucidated the changes occurring.

We shall need a nomenclature for stereoisomerides of the series. Rotenone (I) has three asymmetric carbon atoms, C7, C8, and C20 (the numbering is designed to retain C7 and C8 as they are in the customary system of partial numbering). The junction of rings *B* and *C* may be *cis* or *trans*. Although, by analogy, the *trans*-structure appears more probable for rotenone, we prefer not to dogmatise. We shall call that mode of ring junction present in rotenone the normal form and the other the *allo*-form; we shall designate the latter by the prefix *allo* to the names of substances containing it, whilst substances without this prefix will be understood to have the normal ring junction as present in rotenone. It is apparent that change in the configuration of only one of the atoms C7 and C8 involves also a change from the normal to the *allo*-form or *vice versa*. When once we have decided whether a substance belongs to the normal or the *allo*-series, it suffices for our initial purpose to consider C7 and C8 together as a single asymmetric

centre. We shall define the stereochemistry of the third asymmetric atom, C20, by the absence or presence of the prefix *epi*; when this prefix is absent, the hydrogen atoms

(I.)





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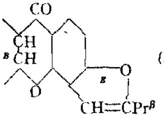


(III.)

attached to C20 and C8 bear the same steric relation to each other as in rotenone. It is inadvisable to relate C20 to C7, since the asymmetry of C7 is destroyed by enolisation.

Rotenone, which is lævorotatory in benzene, is oxidised by iodine, ferricyanide, etc., to *l*-dehydrorotenone (II); in this reaction the asymmetry of C7 and C8 is destroyed and the lævorotation of the dehydro-compound is due solely to C20. It follows that C20 in rotenone is lævorotatory. When rotenone is treated with sulphuric acid, best in acetic acid (Wright, *J. Amer. Chem. Soc.*, 1928, **50**, 3355), it gives *iso*rotenone (III), which is lævorotatory in benzene; in this reaction the asymmetry of C20 has been destroyed, but there is no reason to suppose that C7 and C8 have been affected. It follows that in rotenone C7 and C8, considered as a single asymmetric centre, are lævorotatory. We thus arrive at the nomenclature set out in Table I.

TABLE I.

*Nomenclature of the Stereoisomerides of Rotenone.*

| Prefix. | Asymmetry at C7—C8, normal series. | Asymmetry at C20, normal series. | Racemic forms. | Prefix. | Asymmetry at C7—C8, *allo*-series. | Asymmetry at C20, *allo*-series. | Racemic forms. |
|---|---|---|---|---|---|---|---|
| (nil or *l*-) ........... | *l* | *l* | *dl*- | *l-allo*- ............... | *l* | *l* | *dl-allo*- |
| *d*- ..................... | *d* | *d* | | *d-allo*- ............... | *d* | *d* | |
| *l-epi*- ............... | *l* | *d* | *dl-epi*- | *l-epiallo*- ............ | *l* | *d* | *dl-epiallo*- |
| *d-epi*- ............... | *d* | *l* | | *d-epiallo*- ......... | *d* | *l* | |

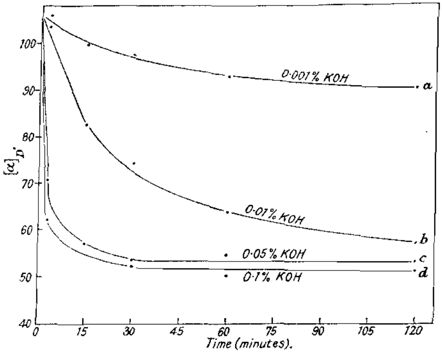
For *iso*rotenone, deguelin, and other substances in which there is no asymmetry in ring *E*, we have the simpler case of *l*-, *d*-, and *dl*-normal and *l*-, *d*-, and *dl-allo*-forms. We note also that dehydro-compounds cannot exist in normal and *allo*-forms, so that there can exist only inactive dehydro*iso*rotenone and *l*-, *d*-, and *dl*-dehydrorotenone.

In this scheme we follow the method used in the sterol series. We refer all rotations to benzene solutions, not for any theoretical reason, but because we find it convenient; the necessity for specifying the solvent will appear later. The prefix *l*- or *d*- for the four *epi*-compounds is fixed by the rotation at the C7—C8 centre and may not coincide with the sign of the total rotation. It should be noted that the rules of simple optical superposition do not apply in this series; for instance, *l*-dehydrorotenone has $[\alpha]_D$ −77° and *l-iso*rotenone has $[\alpha]_D$ −73°, whereas rotenone, containing only the asymmetric centres of these two substances, has $[\alpha]_D$ −226° (all in benzene). Finally we have neglected isomerism which would arise if rings *B* and *C* were not planar; LaForge and Haller [(*b*) *J. Amer. Chem. Soc.*, 1934, **56**, 1620] have envisaged this possibility, but we consider it no longer necessary (*vide infra*).

When 1 c.c. of 1—10% ethyl-alcoholic potassium hydroxide is added to 4 g. of rotenone in 100 c.c. of acetone, the rotation falls rapidly; the rate depends on the amount of alkali

used, as shown in Fig. 1, but, except in very weak solutions, an equilibrium is rapidly reached, the final value remaining constant for many hours. The reaction mixture contains small amounts of oxidation products, but the bulk of the product is a new substance, m. p. 146°, $[\alpha]_D$ −83° in benzene, which we term *mutarotenone*; analysis shows it to be isomeric with rotenone. The same substance is formed by the Tattersfield–Martin procedure mentioned above and also by heating rotenone with an alkali acetate in absolute or 96% alcohol or with anhydrous potassium carbonate in acetone containing 1—2% (not less or much more) of water. The effect of rather vigorous or exceedingly mild alkaline conditions is thus the same. The product, mutarotenone, is, however, not a single substance. Nearly half its weight of rotenone separates as the crystalline solvate containing one molecule of carbon tetrachloride of crystallisation when mutarotenone is dissolved in this solvent. The mother-liquors yield a gum, which we have been unable to crystallise; but we are able to state its composition with complete certainty.

Fig. 1.




*Change of* $[\alpha]_D$ *with time when* 1 *c.c. of* (a) 0·1%, (b) 1%, (c) 5%, *and* (d) 10% *ethyl-alcoholic potassium hydroxide solution is added to* 4 *g. of rotenone in* 100 *c.c. of acetone. Percentages stated on the curves are the* % KOH *in the total solution.*

With iodine, mutarotenone gives an almost quantitative yield of *l*-dehydrorotenone (II), showing that all the components of the compound have a lævorotatory C20, whilst isomerisation by sulphuric acid gives *dl-iso*rotenone (III), showing that only normal ring-forms are present and that the C7—C8 centre is present in mutarotenone in equal amounts of *d*- and *l*-forms. Half of mutarotenone is rotenone, in which both C20 and C7—C8 are lævorotatory; the other half must, therefore, be the isomeride of the normal series in which C20 is lævorotatory and C7—C8 dextrorotatory, that is, *d-epi*rotenone. Mutarotenone is then a 1 : 1 molecular compound of rotenone and *d-epi*rotenone, a kind of semi-racemic compound. Rotenone separates from carbon tetrachloride because it forms a solvate, whereas *d-epi*rotenone (which is not the enantiomorph of rotenone) apparently does not, but in other solvents no separation has been observed.

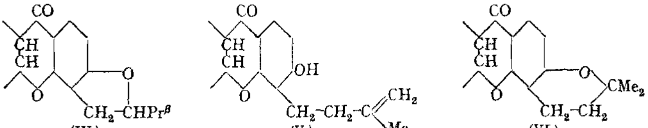
The purity of mutarotenone cannot be judged by its melting point, which varies only slightly on recrystallisation; optical rotation is, however, a satisfactory guide to purity, for material with $[\alpha]_D$ −83° in benzene gives *iso*rotenone which is optically inactive in the crude state, whereas material having about the same melting point but a higher rotation gives slightly active crude *iso*rotenone, from which the activity departs on purification.

Since rotenone has $[\alpha]_D$ −226° in benzene and mutarotenone has $[\alpha]_D$ −83°, *d-epi*-rotenone is expected to have $[\alpha]_D$ +60° in benzene. The highest rotation observed for

our gummy material is +30°. We have also been unable to prepare a crystalline derivative of *d-epi*rotenone, *e.g.*, an oxime; the structure assigned to it is, however, confirmed by hydrogenation, isomerisation by sulphuric acid, and by the fact that racemisation of C7 and C8 is a general reaction. Potassium carbonate in acetone or sodium acetate in alcohol provides, in fact, the readiest method of preparing inactive *iso*rotenone, dihydrodeguelin, and rotenonic acid (*iso*dihydrorotenone) from their active isomerides—in these three compounds only C7 and C8 are asymmetric.

Isomerisation of our gummy *d-epi*rotenone yielded readily and in quantity d-*isorotenone*, m. p. 182°, $[\alpha]_D$ +75° in benzene, −10° in acetone. This is obviously the enantiomorph of the known *l-iso*rotenone, m. p. 184°, $[\alpha]_D$ −73° in benzene, +7·5° in acetone; we confirmed this by preparing *dl-iso*rotenone, m. p. 170°, identical (mixed m. p.) with an authentic specimen (m. p. 170°), by crystallising together equal parts of the *d*- and the *l*-form, and observing that 1 : 2 and 2 : 1 mixtures of the active forms melted at about 165°. Clearly, then, the main component of our *d-epi*rotenone has a dextrorotatory C7—C8 centre.

The results of hydrogenation of *d-epi*rotenone would in themselves provide a complete proof of structure, but the yields are poor and we base our proof on the other reactions mentioned, in all of which excellent yields are obtained. Hydrogenation of rotenone under various conditions gives the dihydro-compounds, dihydrorotenone (IV) and rotenonic acid (*iso*dihydrorotenone) (V), or the fully reduced phenolic tetrahydro-compound, according to the conditions [Kariyone, Kimura, and Kondo, *J. Pharm. Soc. Japan*, 1924, **514**, 1049. LaForge and Smith, (*c*) *J. Amer. Chem. Soc.*, 1929, **51**, 2574. Takei, Miyajima, and Ōno, *Ber.*, 1933, **66**, 479; *Bull. Inst. Phys. Chem. Res. Tokyo*, 1933, **12**, 239. Haller and Schaffer, (*d*) *J. Amer. Chem. Soc.*, 1933, **55**, 3494; (*e*) *Ind. Eng. Chem.*, 1933, **25**, 933]. *l*-Rotenonic acid (V) is cyclised by sulphuric acid to *l*-dihydrodeguelin (*l*-β-dihydrorotenone) (VI), m. p. 156°. The phenol (V) is best obtained by the

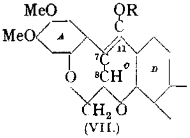



(IV.) (V.) (VI.)

use of platinum in alkaline solution, but, when the amount of alkali is increased sufficiently to give reasonable yields, racemisation also occurs. We needed a method of preparing the active phenol in quantity, and after some experimentation (see p. 527) found it in hydrogenation in dioxan in the presence of palladised barium sulphate and potassium acetate. We would remark, in passing, that racemisation by hot, fairly concentrated alkali has been well established for some time [Haller and LaForge, (*f*) *J. Amer. Chem. Soc.*, 1931, **53**, 3426 and *a*], but that this racemisation by traces of alkali in the cold during hydrogenation (Takei *et al.*, *loc. cit.*, 1933), fully comparable with our conditions of racemisation, has hitherto passed without comment. We hydrogenated, by the methods thus available, the purest *d-epi*rotenone which we could obtain; by using Adams's catalyst in ethyl acetate, we got d-*dihydro*epi*rotenone* (IV), which, as anticipated, is not enantiomorphic with *l*-dihydrorotenone (IV). With palladised barium sulphate and potassium acetate in dioxan we got a phenolic gum, which we believe to have been impure *d*-rotenonic acid (V), since cyclisation yielded d-*dihydrodeguelin* (d-*dihydro*-β-*rotenone*) (VI), m. p. 154°; we had insufficient of this material for accurate determination of the rotation, but a definite dextrorotation was observed, and identification was rendered certain by the facts that the crystallo-optical data were identical with those of the authentic *l*-form and that crystallisation of equal parts of the *l*- and the *d*-form together gave the higher-melting *dl*-form, m. p. 173°, which did not depress the m. p. (176°) of the authentic *dl*-form and was crystallo-optically identical with it.

We turn now to the mechanism of the racemisation. It is natural to assume that the

first step is enolisation, since a number of enolic acetates (VII; R = Ac) have been known for some time [Smith and LaForge, (*g*) *J. Amer. Chem. Soc.*, 1932, **54**, 2996]. Enolisation of rotenone to (VII; R = H), followed by ketonisation, could not, however,



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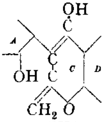

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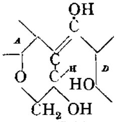
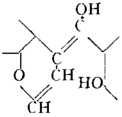


(IX.)

racemise C8, but would merely equilibrate the normal with the *allo*-form. To account for racemisation of C7 and C8 we have considered the three intermediates of types (VIII), (IX), and (X). We can exclude (VIII), because our experiments with toxicarol show that fission of ring *C* occurs. We rule out (IX), because Professor Robertson has told us (private communication) that ring closure and opening of dihydroxy-compounds of this type are not sufficiently facile. We conclude, therefore, that racemisation proceeds by way of (X), ring fission being initiated by enolisation. This ring fission is not a novel



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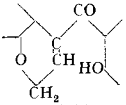

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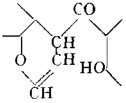


(XII.)

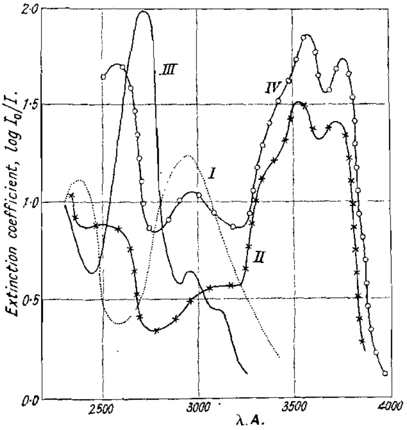
conception. Butenandt and Hilgetag (*Annalen*, 1932, **495**, 172) considered a formula of type (XI) for toxicarol, but the case for the ring-closed formula now generally accepted has been clearly stated by George and Robertson (J., 1937, 1535). In a later paper Butenandt and Hilgetag (*Annalen*, 1933, **506**, 158) suggested that a little of the form (XII) exists in alkaline solution in equilibrium with the ordinary closed-ring form; their reasons were, however, not conclusive, for they rested mainly on the formation of minute yields of certain degradation products. We consider the ketonic form (XII) an extremely unlikely product, for fission of ring *C* would give the αβ-unsaturated ketone (XI) rather than (XII); but (XI) is not a suitable intermediate for the degradations discussed by Butenandt and Hilgetag. The enolic form (X) of (XII) is free of all objections and our experiments confirm the validity of Butenandt's degradative mechanisms. If it is agreed that (X), but not (XI) or (XII), is the intermediate, then the necessity for enolisation prior to ring fission is apparent.

We have discovered the hitherto unsuspected fact that racemisation accompanies formation of the enolic acetyl derivatives. Smith and LaForge (*g*), who prepared acetyl-*iso*rotenone from *l*-*iso*rotenone, did not determine its rotation. Under suitably modified conditions (milder than those used by Smith and LaForge, so that no objection can be raised on this score), *l*-*iso*rotenone gives a 75% yield of inactive acetate, which is obtained also from *dl*-*iso*rotenone and regenerates *dl*-*iso*rotenone when hydrolysed by dilute acid—dilute acid does not cause racemisation. Haller and LaForge (*a*) report hydrolysis of the acetate to an *iso*rotenone having $[\alpha]_D$ −21·1° in benzene, ordinary *l*-*iso*rotenone having $[\alpha]_D$ −73°; this was presumably due to their acetate having contained some unacetylated material. Acetylation of rotenone presents a more complicated picture. In acetyl*iso*rotenone, only C8 is asymmetric and racemisation thus gives a true *dl*-compound. In acetylrotenone, C20 retains its asymmetry; acetylation of rotenone, accompanied by racemisation of C8, must yield a mixture unless acetyl-*l*-rotenone and acetyl-*d*-*epi*rotenone form a molecular compound analogous to mutarotenone. No such compound appears to be formed. The crystalline product isolated is acetyl-*l*-rotenone and not the *epi*-compound, since it gives on hydrolysis an excellent yield of ordinary rotenone of unchanged

rotation. However, the crystalline compound is accompanied by much gummy material, and, since there is no reason to expect rotenone and *iso*rotenone to behave differently, it is at least possible to connect the gummy by-product with the presence of the *d-epi*-compound.

The mechanism of racemisation during acetylation is obscure; and the position is further complicated by anomalous acetylation, of the isomerides of toxicarol (see pp. 528, 533, 534). If racemisation occurred in this case also by way of the "open" form (X), one would expect to obtain substances in which the phenolic hydroxyl group was acetylated. The enolic acetate structure (VII; R = Ac) was, however, proved by Smith and LaForge (*g*), who hydrogenated acetylrotenone to dihydrodeoxyrotenone in which the >C:C·OAc group has been reduced to $>CH\cdot CH_2$. The structure (VII) is confirmed by absorption spectra. In Fig. 2 we show the absorption spectra of

FIG. 2.
*Absorption spectra. Alcoholic solutions.*



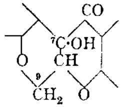

I, *Rotenone* 0·00302%, 1 *cm*. III, *Toxicarol* 0·00239%, 1 *cm*.
II, *Acetylrotenone* 0·00222%, 1 *cm*. IV, *Diacetyltoxicarol* 0·00335%, 1 *cm*.

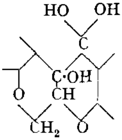
rotenone, acetylrotenone, toxicarol, and diacetyltoxicarol. We shall discuss toxicarol and its acetate later. At this point we would note merely that in the acetates the main absorption maxima are displaced nearly into the visible region; this indicates a series of six or seven conjugated ethylenic linkings, which is provided in (VII) by the aromatic rings *A* and *D* united by the C7—C11 ethylenic linking. In rotenone and toxicarol the system Ar·C:C·Ar is replaced by Ar·CH·CO·Ar and the principal absorption maxima are in regions of much shorter wave-length. Finally, hydrolysis of acetylrotenone gives a 83% yield of rotenoue and not mutarotenone; the latter would be produced if the acetate were a derivative of the "open" form (X).

One further aspect calls for comment at this point. Acid hydrolysis of the enolic acetates gives excellent yields of the parent ketones. This regenerates the asymmetry of C7, but no signs of acid conditions affecting C8 have been observed. We should thus expect hydrolysis to produce mixtures of normal and *allo*-forms; actually normal forms are obtained in all cases in excellent yields (as has just been mentioned for acetylrotenone),

and *allo*-forms could not be detected. In alkaline reactions, too, no *allo*-forms were isolated, but in these cases yields are not so good and the conditions are consequently less searching. It is clear that steric relations favour the normal to the complete or nearly complete exclusion of the *allo*-form and that newly formed asymmetry at C7 is determined by any asymmetry already existing at C8. There is a partial analogy, kindly pointed out to us by Dr. S. H. Harper, in that *cis*-α-decalone passes readily and apparently irreversibly into the *trans*-isomeride (Hückel, *Annalen*, 1925, **441**, 1).

This generalisation requires qualification in one respect. Oxidation by air or hydrogen peroxide in the presence of alkali gives a series of hydroxy-derivatives (LaForge and Haller, *b*, who give earlier references). Some, at least, of these are pairs of 7-hydroxy-derivatives (XIII), doubtless obtained by way of (XIV), which arises by 1 : 2 addition of 2OH to

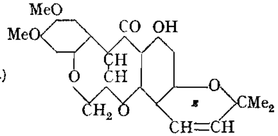
(XIII.) 

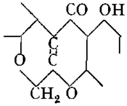

 (XIV.)


(X); it is suggestive that in these apparently well-authenticated cases of normal and *allo*-forms interconversion by enolisation is impossible. LaForge and Haller considered that non-planar configurations of rings might be necessary to account for other isomerides discovered, but we see now that 1 : 4 addition to (X) might lead to 9-hydroxy-derivatives, two of which could exist by virtue of the new asymmetry at C9. Further work on these interesting substances is desirable.

### B. *Action of Alkali on Toxicarol.*

Elegant proof of the structure of toxicarol (XV) has finally been provided by Robertson and his co-workers (*J.*, 1937, 1535 and earlier papers). When toxicarol (which is optically inactive) is heated with potassium carbonate in acetone, it is partly changed into an isomeride, which we term β-*toxicarol*, the two substances being readily separable by reason of the much greater solubility of the new compound in ether. The reaction is reversible,

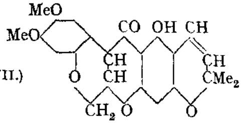
(XV.) 

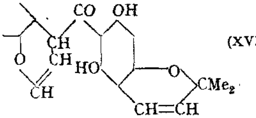

 (XVI.)


the new compound being partly reconvertible under the conditions of its formation into ordinary toxicarol (we shall term this α-toxicarol when we need to contrast it with the new isomeride, but shall otherwise omit the prefix). β-Toxicarol is equilibrated also by alcoholic alkali, but in this case the much less soluble α-toxicarol crystallises, so that in alcohol the change β → α is almost complete. The α-toxicarol which has separated after the solution has cooled contains, however, some of the β-isomeride and this largely accounts for the various melting points reported for α-toxicarol prepared from *Derris* extracts [213° by Butenandt and Hilgetag, *loc. cit.*, 1932; 219° (corr.) by Clark, *a*; 220° by Cahn and Boam, *loc. cit.*]; if α-toxicarol prepared from the extract is subjected to purification by the ether method, the melting point rises at once to 226° and subsequent crystallisation raises it to 232—233°; repeated crystallisation from acetic acid or benzene is needed if the ether purification is omitted. The removal of β-toxicarol can be followed quantitatively by the Goodhue colour test (*J. Assoc. Off. Agric. Chem.*, 1936, **19**, 118), which is given by β- but not by α-toxicarol; we find that α-toxicarol of m. p. 219° contains 4·5% of the β-isomeride.

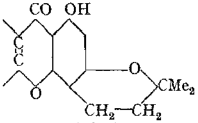
We had to consider two possibilities for the structure of β-toxicarol. The first, that it

was the *allo*-form of toxicarol, was readily eliminated, since oxidation of β-toxicarol gives a dehydro-compound (XVI), which is not identical with ordinary dehydrotoxicarol. The alternative was the linear form (XVII). George and Robertson (*loc. cit.*) have pointed out that (XVIII) is an intermediate common to (XV) and (XVII). Professor Robertson had mentioned this in conversation with one of us (R. S. C.) earlier and before the discovery of β-toxicarol, and realisation of the relationship greatly simplified elucidation of the structure

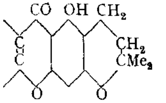
(XVII.) 


 (XVIII.)

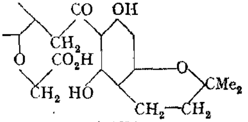

of this compound. Now (XVIII) (or, rather, its enolic equivalent) is the form which, by analogy with rotenone, we should expect toxicarol to assume in the presence of alkali, and equilibration of (XV) and (XVII) by alkali would be in line with our experiences in the rotenone series. This interpretation was readily proved correct. Hydrogenation of toxicarol in acetic acid at 75° [Clark, (*f*) *J. Amer. Chem. Soc.*, 1931, **53**, 2264] or, as we find, more conveniently in dioxan at room temperature, gives dihydrotoxicarol, in which ring *E* is saturated. Oxidation then gives dehydrodihydrotoxicarol (XIX). β-Toxicarol gives similarly the isomeric *dihydro*-β- and *dehydrodihydro*-β-*toxicarol* (XX). When heated with potassium hydroxide, (XIX) gives dihydrotoxicarolic acid (XXI) (Clark, *d*).




(XIX.)




(XX.)




(XXI.)

Dehydrodihydro-β-toxicarol gives the same acid (XXI), identified by the melting points and mixed melting points of the acid, its ester, and ester diacetate. This is explicable only if dehydrodihydro-β-toxicarol has the structure (XX), which necessitates formula (XVII) for β-toxicarol. The interconversion of (XVII) and (XV) proves that fission of ring *C* occurs under the influence of alkali, which in turn is very strong support for the mechanism postulated by us for racemisation.

As was the case with rotenone, toxicarol reacts in the closed form (XV) when acetylated. Mild treatment gives a monoacetate, in which only the phenolic hydroxyl group is acetylated. More drastic treatment gives excellent yields of a diacetate, analogous to acetylrotenone, the structure of which is proved in the same way. First, Clark (*f*) hydrogenated diacetyltoxicarol to acetyldeoxydihydrotoxicarol. Secondly, the absorption spectrum of diacetyltoxicarol shows the three-banded maximum characteristic of acetylrotenone as shown in Fig. 2 (these and other absorption data are discussed further in the experimental portion, p. 535). Finally, hydrolysis of diacetyltoxicarol by dilute acid gives a quantitative yield of α-toxicarol, with no trace of β-toxicarol or of *allo*-forms.

Two further theoretical points follow. First, the quantitative hydrolysis of diacetyltoxicarol to α-toxicarol shows that *allo*-forms are as little favoured in the toxicarol as in the rotenone series, and, secondly, this hydrolysis and that of acetylrotenone are experimental justification for our contention that dilute acid does not affect C8.

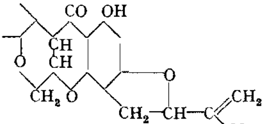
Clark (*d*) obtained acetyldehydrotoxicarol by ring-closure of (XXI) by acetic anhydride. George and Robertson (*loc. cit.*) saw that this reaction should give a mixture of the acetates of (XIX) and (XX) and isolated a little of a compound, m. p. 238—239° (*decomp.*), which they thought might be (XX) [they termed the then hypothetical (XVII) *iso*toxicarol, but we prefer to use the prefix *iso* only for isomerism of the rotenone–*iso*rotenone type]; however, (XX) has m. p. 226—227°; George and Robertson's compound may have been

impure dehydrodihydro-α-toxicarol (XIX), which has m. p. 260°. Knowing that *acetyldehydrodihydro-β-toxicarol*, readily obtained from (XX), is more soluble than its α-isomeride, we had independently searched for it in the mother-liquors obtained in this reaction; we failed to find it there.

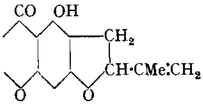
C. *The Toxicarol Precursor.*

Tattersfield and Martin (*locc. cit.*) isolated their toxicarol precursor by crystallising from ethyl acetate either the whole or the alkali-soluble part of a Sumatra-type *Derris* extract (*i.e.*, an extract giving much toxicarol with alkali). Our difficulties connected with this substance were confined to its isolation and purification. At first we could not isolate it at all, but after Dr. Tattersfield had very kindly provided us with samples, we were able to obtain crystals from ethyl acetate–alcohol or ether; ethyl acetate alone could not be used until after preliminary purification. Plain recrystallisation gave material identical with that of Tattersfield and Martin in m. p. and rotation ($[\alpha]_D$ −68° in benzene), but analyses were unintelligible, values for carbon being 0·5—1·4% low for toxicarol, even after thorough drying. Proof that the material was heterogeneous came by acetylation, which gave very poor and erratic results; in one experiment a small amount of a *monoacetate*, m. p. 158°, of the precursor was obtained; in others a little *monoacetylsumatrol*, m. p. 217°, was isolated, which gave sumatrol on hydrolysis by acid and was also obtained (m. p. 218—219°) in 60% yield by gentle acetylation of sumatrol [Cahn and Boam (*loc. cit.*) and Robertson and Rusby (*loc. cit.*) were unable to crystallise acetylsumatrol]. After long trials we found that the sumatrol could be separated by stirring with an insufficiency of pure ether. Our final product had $[\alpha]_D$ −53° in benzene, but had the same m. p., 101—102°, as before removal of the sumatrol, which melts at 189°. It now gave correct analytical results for $C_{23}H_{22}O_7$ (toxicarol). The low analytical figures for carbon obtained for the earlier product cannot have been caused by the sumatrol, which is isomeric with toxicarol and crystallises from alcohol or ethyl acetate without solvent of crystallisation; it seems that a third substance must have been present, in which case the constancy of the m. p. appears still more remarkable. We should add that sumatrol has an asymmetric atom, C20, not present in the precursor and that the sumatrol isolated has its full activity; progressive change of the precursor into sumatrol is thus impossible.

Tattersfield and Martin (*locc. cit.*) found that, when methyl-alcoholic potassium hydroxide was added to a benzene solution of their precursor, $[\alpha]_D$ −70° in benzene, the initial small lævorotation changed immediately to a powerful dextrorotation, +300° to +321° after 2 minutes, and then sank slowly. Our material, $[\alpha]_D$ −68°, behaved similarly, but material having $[\alpha]_D$ −53° gave a dextrorotation of +350°, which sank later to exactly zero. Under Tattersfield–Martin conditions sumatrol, which is almost certainly 15-hydroxyrotenone (XXII) [the only alternative (XXIII) is much less probable (George and Robertson, *loc. cit.*; *cf.* also the evidence of absorption spectra, p. 535)], changes its rotation, −158°, instantaneously to +105°, which falls slowly through zero to −42°; the final rotation is due to C20, for we have seen in the rotenone series that under Tattersfield–Martin conditions only C7 and C8 are racemised—we shall discuss the change of sign later. This indicates that Tattersfield and Martin's material, $[\alpha]_D$ −70°, resembled our material, $[\alpha]_D$ −68°, and so probably contained sumatrol. The final fall of α of our




(XXII.)




(XXIII.)

material to absolutely nil proves its freedom from sumatrol and that the precursor has no asymmetry beyond that of C7 and C8.

Once purity had been attained, we readily proved the precursor to be *l-α-toxicarol.*

With alcoholic alkali it gives excellent yields of ordinary α-toxicarol, as was found for the impure material by Tattersfield and Martin. With methyl-alcoholic potassium hydroxide and benzene, potassium carbonate in acetone, etc., it gives a mixture of inactive α- and β-toxicarol. These reactions, together with the analytical figures, prove the precursor to be one or other active form of α- or β-toxicarol. The next step, proof that it belongs to the α-series, is provided by its oxidation to dehydro-α-toxicarol and its hydrogenation to l-*dihydro-α-toxicarol*, which is oxidised by iodine to dehydrodihydro-α-toxicarol.

This chemical evidence is confirmed by the absorption spectrum of the precursor, which is almost identical with that of *dl*-α-toxicarol.

We must next consider the meaning of the change in sign of rotation under Tattersfield–Martin conditions. If the alkaline, dextrorotatory solution is acidified before the decline to zero commences, *l*-toxicarol is recovered with unchanged rotation, $[\alpha]_D$ −53° in benzene. This disposes of the possibility that, in spite of the analytical figures, the precursor is really some labile compound of an active toxicarol and that the remarkable change in sign of rotation is due to liberation of active toxicarol from such a compound; this possibility is further discounted by the exactly analogous behaviour of sumatrol, the structure of which is beyond doubt. Actually we believe the instantaneous changes in sign are adequately explained by enolisation and this leads to further interesting conclusions. When *l*-toxicarol is enolised by the potassium hydroxide, the asymmetry of C7 is destroyed, but that of C8 remains; the optical behaviour is explained if C7 is lævorotatory and C8 dextrorotatory, the contribution of C7 being numerically greater than that of C8; the final fall to zero is caused by racemisation also of C8, which we believe proceeds by way of the "open" form. We explain the behaviour of sumatrol similarly; the final fall of $[\alpha]_D$ to −42° shows C20 to be lævorotatory; C8 is dextrorotatory and C7 strongly lævorotatory. We notice that with *l*-toxicarol the orientation of C8 determines the orientation of the hydrogen atom returning to C7, since the *l*-toxicarol regenerated from the enol has its full optical rotation, behaviour which is exactly parallel to the hydrolysis of acetylrotenone. We note further that the opposing signs of the rotations due to C7 and C8 afford a rational explanation of *l*-toxicarol being lævorotatory in benzene and dextrorotatory in acetone—for the relative numerical contributions of different asymmetric centres may well vary in different solvents.*

The rotation of rotenone shows no immediate change under Tattersfield–Martin conditions, but only the slow change due to racemisation. This indicates in our opinion that rotenone is less easily enolised than is toxicarol. This is endorsed by the absorption spectra data. Thus, the absorption of rotenone in alcohol is unchanged by the addition of 1% of sodium hydroxide. Alkali immediately changes the colour of toxicarol solutions from yellow to orange-yellow; the displacement of the absorption maximum to longer wave-lengths (cf. data, p. 535) is in agreement with conjugation of the C7—C11 ethylenic linking with the two aromatic rings *A* and *D* consequent upon enolisation. There is also evidence, more convincing than that of Butenandt and Hilgetag (*loc. cit.*), that the ring-fission which follows enolisation is more facile in the toxicarol than in the rotenone series, but we reserve this work for a later communication.

Owing to the incomplete enolisation we cannot allocate definite signs of rotation to C7 and C8 in rotenone. Rotenone is lævorotatory in all solvents tried; but *iso*rotenone is lævorotatory in benzene and dextrorotatory in acetone, dioxan, or chloroform, behaviour which we accounted for in the case of *l*-toxicarol by the opposing contributions of C7 and C8. It is thus probable that in *iso*rotenone and, therefore, in rotenone C7 and C8 have rotations in opposite directions; in rotenone C20 is also lævorotatory, so that the total rotation is negative in all solvents.

One point of the structure of the toxicarol precursor has been left unsettled above, namely, whether it is a normal or *allo*-form. Now, we have seen from the hydrolysis of diacetyltoxicarol that ketonisation of the enolic form gives only the normal keto-form; if we are correct in interpreting the change in sign of rotation in alkaline solution as due to enolisation, then the precursor must be the normal form of *l*-α-toxicarol; for, if it were an *allo*-form, enolisation by alkali, followed by immediate acidification, would lead to a new

* This invalidates the complicated calculations of Jones (*J. Agric. Res.*, 1936, **53**, 831).

compound having the stable normal ring structure, and we have seen that this does not occur.

*l*-Toxicarol can be isolated by direct crystallisation from Sumatra-type extract or by first extracting the ethereal solution of the extract with aqueous alkali and then crystallising the phenolic portion. These two methods give products which are chemically indistinguishable, and identity was confirmed by crystallo-optical comparison of material isolated by each method and purified to the $[\alpha]_D$ −68° stage. This identification was necessary in view of the known effects of alkali.

The remarkable difference in melting point and solubility between *l*- and *dl*-α-toxicarol, as well as the difficulty of purifying the *l*-form, might be held to indicate that the toxicarol precursor is in fact a mixture; while we cannot exclude definitely the existence of, *e.g.*, other steric forms, there is no valid evidence at all of the occurrence of more than one precursor.

Finally we would point out the dependence of the rate of racemisation on the solvent used. No racemisation occurs when an ethereal solution of *Derris* extract is shaken for a short time with aqueous alkali; in benzene, the rate is greatly accelerated by large additions of methyl alcohol, but even then large amounts of alkali hydroxide appear to be needed. In acetone containing 1% of ethyl alcohol, traces of alkali hydroxide suffice; and when potassium carbonate in acetone is used, the permissible water content is restricted to about 1—2%. Alkali acetates are effective in 96% or absolute ethyl alcohol, even after addition of a little acetic acid. Lastly, Merck's or B.D.H.'s "activated alumina for adsorption," which has been shown to contain unexpectedly large amounts of adsorbed alkali (Cahn and Phipers, *Nature*, 1937, **139**, 717), racemises rotenone derivatives in benzene or chloroform. Thus chromatographic adsorption of *l*-α-toxicarol gave some *dl*-α-toxicarol (the more soluble β-isomeride could not be separated from unchanged *l*-toxicarol), and rotenone was partly converted into a gummy material (this was observed before the discovery of mutarotenone; doubtless *d-epi*rotenone was formed, but we did not confirm this by experiment).

## Experimental.

The *Derris* extracts used were commercial extracts; in order to define the materials, Goodhue and ferric chloride values are stated; the meaning of these terms will be explained elsewhere. Owing to the variability of *Derris* extract, workers using other raw material should expect qualitatively, but not quantitatively, similar results. Analyses are by Dr. G. Weiler, Oxford, except methoxyl determinations, which, unless otherwise stated, were done by us by Clark's volumetric semi-micro method (*J. Assoc. Off. Agric. Chem.*, 1932, **15**, 136), using a simplified apparatus. Macro-methods of determining methoxyl are unsatisfactory in this series; micro-methods are better, but, we find, not always as reliable as that used. Optical rotations are only approximate, as unfortunately no accurate polarimeter was available; we, therefore, omit references to temperature and concentrations. In experiments on racemisation the acetone used was B.D.H.'s "Acetone, redistilled," unless otherwise specified; this material usually contained just sufficient water to allow racemisation, but addition of 1% of water was, however, needed for some samples.

*Mutarotenone.*—(*a*) Rotenone (10 g.) and anhydrous potassium carbonate (20 g.) in acetone (100 c.c.) were heated under reflux for 2 hours. The filtered solution and washings from the carbonate were acidified with acetic acid and evaporated. The residue, crystallised from alcohol, gave 8·3 g., m. p. 137—140°, which on recrystallisation afforded 5·4 g. (*A*), m. p. 141—145°, $[\alpha]_D$ −103° in benzene. Concentration of the filtrates gave 0·1 g. of dehydrorotenone, m. p. 229—233°, identified by a mixed m. p. determination and its failure to give the Durham reaction (a useful diagnostic in this and similar cases); evaporation to dryness gave a gum, which in ether deposited first 0·3 g. of indefinite material and then pale yellow crystals (0·8 g.), m. p. 145—150°. An alcoholic solution of (*A*) deposited first 0·05 g. of dehydrorotenone, later (overnight) 1·8 g. of mostly colourless crystals, and, when concentrated, a further 2·8 g. of similar crystals. Fractional extraction of the two last fractions (bulked) with hot alcohol removed preferentially a lævorotatory component, probably rotenone; the first fraction (1·7 g.) had m. p. 141—142°, $[\alpha]_D$ −120° in benzene, the second (*B*) (1·6 g.) had m. p. 145—146°, $[\alpha]_D$ −100° in benzene, and concentration of the combined mother-liquors gave (*C*) (0·5 g.), m. p. 141—145°. Addition of ether (100 c.c.) to (*B*) and (*C*) in the least amount of benzene caused crystallisation

of pure *mutarotenone* (1·2 g.), m. p. 146—148° (Found : C, 69·6; H, 5·8. $C_{23}H_{22}O_6$ requires C, 70·0; H, 5·6%). Concentration of the ether–benzene mother-liquors gave first rotenone (0·25 g.) (prisms, m. p. 164° alone or mixed with an authentic specimen) and then material (1·5 g.), $[\alpha]_D$ −120°, which by crystallisation from ether–benzene gave a further 1·2 g. of pure mutarotenone. For pure mutarotenone, which separates from ether or alcohol in clusters of fine, colourless needles, m. p. 145—146°, $[\alpha]_D$ was variously determined as −80° to −86° in benzene and −37° in acetone.

In pilot experiments rotenone was recovered unchanged when the acetone contained 0, 0·25, or 0·5% of water and only partly racemised when the water content was 5 or 10%.

(*b*) 1% Alcoholic potassium hydroxide (25 c.c.) was added to rotenone (50 g.) in acetone (1 l.), and the whole kept under coal gas for 6 hours. A slight excess of acetic acid was added, the solvents removed, and the residue stirred with warm alcohol (400 c.c.). After cooling, the pale yellow crystals (41·5 g.), m. p. 140—142°, $[\alpha]_D$ −115° in benzene, were collected and fractionally extracted with two 200 c.c. portions of hot alcohol; the alcohol deposited (i) 4·5 g., m. p. 143—144°, $[\alpha]_D$ −118°, and (ii) 9 g., m. p. 145—146°, $[\alpha]_D$ −100° in benzene. The less soluble residue, crystallised from alcohol–benzene, gave nearly pure mutarotenone (21·5 g.), m. p. 145—146°, $[\alpha]_D$ −87°, which was finally purified (17·5 g.) to $[\alpha]_D$ −80° in benzene by twice adding ether (200 c.c.) to its solution in the minimum amount of benzene. Fractions (i) and (ii) were dissolved in the least amount of acetone and poured into a mixture of ether and water; the ethereal layer was rapidly filtered from dehydrorotenone (2·5 g.), m. p. 229—231° after recrystallisation, identified as above, and then deposited crystals (4·5 g.), m. p. 147—148°, $[\alpha]_D$ −163° in benzene, which by treatment with carbon tetrachloride gave 69% of rotenone and a residual gum having $[\alpha]_D$ +3° in benzene.

(*c*) Rotenone (1 g.) and anhydrous sodium acetate (3 g.) in alcohol (20 c.c.) were heated under reflux for 2 hours. The product which separated on dilution with water had $[\alpha]_D$ −82° in benzene and on recrystallisation gave mutarotenone (0·72 g.), m. p. 143—145°, $[\alpha]_D$ −72°. Similar experiments with potassium acetate in absolute and in 96% alcohol gave substantially similar results. These are much the most convenient methods of preparing mutarotenone, as no dehydro-compounds are formed and purification is thus simpler, but we have not practised them on a larger scale.

Pyridine also racemises the C7—C8 system. When pyridine (10 c.c.) was added to rotenone (2·5 g.) in acetone (50 c.c.), $[\alpha]_D$, originally −106°, fell to −95° in 5 minutes and −80° in 1 hour, but then remained constant overnight. When rotenone (1 g.) was heated in pyridine (5 c.c.) on the water-bath for 1 hour, the product, isolated by pouring the solution into dilute hyrochloric acid, had $[\alpha]_D$ −145° in benzene.

*Oxidation of mutarotenone.* Iodine (1 g.) in alcohol (10 c.c.) was added gradually to mutarotenone (1 g.) and anhydrous sodium acetate (3 g.) in hot alcohol (40 c.c.) and the whole was heated for a further 2 hours. When cold, the solution had deposited dehydrorotenone (0·82 g.), m. p. 228—230° alone or mixed with an authentic specimen and having $[\alpha]_D$ −70° in benzene (this agrees with the correct figure within our experimental error).

*Isomerisation of mutarotenone.* Concentrated sulphuric acid (3 c.c.) was added gradually to mutarotenone (0·5 g.; $[\alpha]_D$ −70° in benzene) in warm acetic acid (5 c.c.) and the resulting solution was poured into water. The precipitate, collected and dried, had no rotation in benzene. Crystallisation from a limited amount of alcohol gave *dl-iso*rotenone, m. p. 163—164°, identified by its giving a blue colour in the Durham reaction and not depressing the m. p. of an authentic sample. A small, less soluble residue, crystallised from alcohol, gave needles, m. p. 218—220°, identified as dehydro-compounds by their yellow colour and failure to give the Durham test; they undoubtedly arose from traces of rotenolones present in the not quite pure mutarotenone.

A sample of mutarotenone (2 g.), having $[\alpha]_D$ −110° in benzene, with acetic acid (16 c.c.) and sulphuric acid (12 c.c.) gave a crude product, $[\alpha]_D$ −23° in benzene, which, when crystallised from alcohol containing a little benzene, gave completely inactive *dl-iso*rotenone (1·7 g.), m. p. 168° alone or mixed with an authentic sample.

d-epi*Rotenone*.—Pure mutarotenone (14 g.) in carbon tetrachloride deposited 8·1 g. (41·5%) of rotenone–carbon tetrachloride solvate, identified by its rotation, $[\alpha]_D$ −217° in benzene (calc. as rotenone; pure rotenone has $[\alpha]_D$ −226°), and by conversion by alcohol into rotenone, m. p. 163—164° alone or mixed with an authentic specimen. Evaporation of the carbon tetrachloride mother-liquors gave a gum (8 g.), having $[\alpha]_D$ +8° in benzene; when kept in ether, this slowly deposited small amounts of mutarotenone, m. p. 144°, $[\alpha]_D$ −83°, and finally gave on evaporation impure *d-epi*rotenone, $[\alpha]_D$ +30° in benzene. As usually obtained, the product gave a reddish-brown colour with alcoholic ferric chloride, but removal of the phenolic

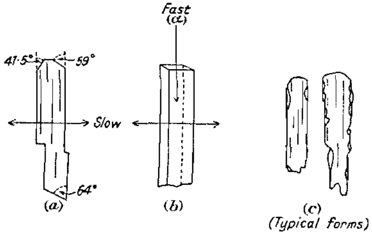
decomposition product with alkali did not lead to a crystallisable material. Attempts to prepare an oxime, hydrochloride, and acetyl derivative gave only gums.

d-iso*Rotenone*.—Crude *d-epi*rotenone [2·8 g., obtained from mutarotenone prepared by method (*b*); $[\alpha]_D$ + 12° in benzene] was treated in acetic acid with sulphuric acid, as described for mutarotenone. The crude product obtained by pouring the reaction mixture into water had $[\alpha]_D$ + 34° in benzene, and, crystallised from alcohol, gave d-iso*rotenone* (1·25 g.) in long, colourless, silky needles, m. p. 182°, $[\alpha]_D$ +75° in benzene, −10° in acetone (Found: C, 70·0; H, 6·1. $C_{23}H_{22}O_6$ requires C, 70·0; H, 5·6%). Mixtures of 1 part of this product with 0·5 and 2 parts of *l-iso*rotenone melted at 166—167° and 165—166°, respectively, but equal weights of the two compounds, crystallised together from alcohol, gave *dl-iso*rotenone, α 0, m. p. 170° alone or mixed with an authentic specimen. *d-iso*Rotenone was similarly obtained from crude *d-epi*rotenone prepared by the potassium carbonate method.

*l-iso*Rotenone has $[\alpha]_D$ about −73° in benzene, +7·5° in acetone, +10° in chloroform, and +12·5° in dioxan.

d-*Dihydro*epi*rotenone* (IV).—Crude *d-epi*rotenone (2·3 g.) in ethyl acetate (25 c.c.) absorbed 130 c.c. of hydrogen in 10 minutes in the presence of a reduced Adams's platinum catalyst (0·25 g.). Hydrogenation was then stopped. The filtered solution was diluted with water, the product was removed by ether and divided into portions soluble and insoluble in aqueous sodium hydroxide. The alkali-soluble part gave only a little gum. The alkali-insoluble part, recovered from the ether, was dissolved in hot alcohol. When cold, the supernatant liquid was decanted from the gum, which had been deposited, and was kept. A small amount of crude d-*dihydro*epi*rotenone*, m. p. 123—125°, slowly separated. Purified by several crystallisations from alcohol, it formed stout prisms, m. p. 127—128°, $[\alpha]_D$ +99° in benzene (Found: C, 69·0; H, 5·9. $C_{23}H_{24}O_6$ requires C, 69·7; H, 6·1%).

FIG. 3.
d- *or* l-*Dihydrodeguelin.*




d-*Dihydrodeguelin* (d-β-*Dihydrorotenone*) (VI).—Crude *d-epi*rotenone (5 g.; $[\alpha]_D$ +25° in benzene) in dioxan (100 c.c.) in the presence of potassium acetate (5 g.) and palladised barium sulphate [5 g.; Houben-Weyl, Vol. 2, p. 270 (1922)] absorbed 260 c.c. of hydrogen in 48 minutes. The solution was filtered, and the inorganic matter thoroughly washed with dioxan. The filtrates were diluted with water and extracted with ether. The ethereal layer, freed from dioxan by several washings with water, was shaken with 5% aqueous potassium hydroxide solution and then retained only uncrystallisable material. The material recovered from the alkaline layer by acidification and extraction with ether, etc., was a gum; test portions decomposed during attempted crystallisation from benzene, benzene-light petroleum, or ether-light petroleum. To one half of the product in acetic acid (5 c.c.) was added concentrated sulphuric acid (20 drops); after 5 minutes the deep red solution was diluted with water and extracted with ether. Uncyclised and other phenolic products were removed with aqueous alkali. The ethereal solution, washed finally with water, dried, and evaporated, gave a gum, from which a pale yellow powder, m. p. 152—153°, was obtained by trituration with a little cold ether. Several crystallisations from methyl alcohol afforded d-*dihydrodeguelin* in colourless prisms (48 mg.), m. p. 154° (Found: C, 69·0; H, 5·6. $C_{23}H_{24}O_6$ requires C, 69·7; H, 6·1%).

*d*-Dihydrodeguelin is crystallo-optically identical with the authentic *l*-form, m. p. 153—154°. Both are colourless, elongated prisms or needles, mainly without good crystal form, but occasionally showing terminations as in Fig. 3*a* and *b*. The extinction in the prism zone is straight; the length direction is fast and this is also the direction of the trace of the optic axial plane. $2V$ is large. $n_D$ are: α (along the length) 1·521, β (across the length) 1·600, γ (across the length) 1·714 (all ±0·002). No etch pits were seen.

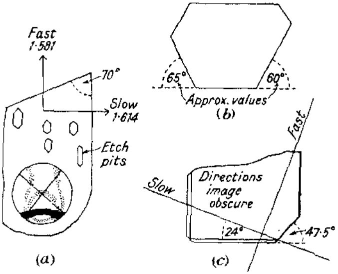
9·5 Mg. each of the *d*- and the *l*-form, crystallised together, gave *dl*-dihydrodeguelin, melting at 173° alone and at 173—174° when mixed with authentic specimens prepared either from deguelin or from *dl*-rotenonic acid. Our product, m. p. 173°, and an authentic specimen were crystallo-optically identical. They form thin, flat plates, mainly of irregular shape, but some-

times showing pseudohexagonal outlines (Fig. 4*b*). In convergent light a very characteristic directions image is presented, one melatope appearing about two-thirds of the distance from the centre of the field to the margin (Fig. 4*a*). The direction of the trace of the optic axial plane is fast. $2V$ is very large. $n_D$, measured on this section, which occurred almost to the exclusion of any other, were: in the direction of the optic plane 1·581; normal to the optic plane 1·614 (both ±0·002). Other sections showed two good cleavages and an obscure directions image, and an occasional section as shown in Fig. 4*c* was seen; the common section is, however, so characteristic that these others are not further described. Almost as characteristic were the etch-pits developed in liquids in which the substance is slowly soluble (*e.g.*, *s*-tetrabromoethane) (see Fig. 4*a*). The pseudo-hexagonal pits are elongated in the direction of the optic axial plane, and are symmetrical about this direction and one at right angles to it. They are formed by the coalescing of two groups of hemimorphic pits oriented parallel to the optic axial plane but in opposite directions.

*Hydrogenation of Rotenone.*—(*a*) l-*Rotenonic acid* (l-*isodihydrorotenone*) (V). Rotenone (10 g.) in " purified " dioxan (200 c.c.) in the presence of potassium acetate (10 g.) and palladised barium sulphate (5 g.; *vide supra*; best freshly prepared and not dried, but washed with dioxan) absorbed 520 c.c. of hydrogen in 95 minutes. The mixture was then treated with much water and 450 c.c. of ether and filtered. The ethereal layer was washed thrice with 5% aqueous potassium hydroxide solution, whereupon the bulk of the sparingly soluble *l*-dihydrorotenone crystallised and was removed by filtration. Acidification of the alkaline washings precipitated *l*-rotenonic acid, which was collected in ether and, after recovery therefrom, was best crystallised from benzene, in which it is sparingly soluble; it formed colourless needles, m. p. 206—208°, $[\alpha]_D$ +46° in chloroform, +49·5° in acetone. Yield, about 45%. Hydrogenation did not occur in technical dioxan.

FIG. 4.

dl-*Dihydrodeguelin.*




(*b*) Our other experiments were not exhaustive, as our object was achieved by discovery of the above method, but a summary of our experiences is of interest. Using Adams's platinum oxide in ethyl acetate, we got 86% of pure *l*-dihydrorotenone and only a trace of phenols; under the conditions of Takei *et al.* (*loc. cit.*) [rotenone (5 g.), alcohol (500 c.c.), 10% aqueous sodium hydroxide (3 c.c.)] we got a very good yield of *dl*-rotenonic acid, m. p. 184°, α 0; hydrogenation of rotenone (5 g.) in alcohol (100 c.c.) containing 1% alcoholic sodium hydroxide (2 c.c.) was slow and incomplete, probably owing to poor quality of the batch of platinum catalyst, but the phenolic part of the product was almost entirely the *dl*-substance; addition of anhydrous sodium acetate (5 g.) to alcohol (100 c.c.) gave only a trace of phenols. Using palladised barium sulphate, we got only traces of phenols from 2 g. of rotenone by adding potassium carbonate (2 g.) to acetone or dioxan (40 c.c.); potassium acetate in acetone led to 11·5% of the active phenol; addition of water to the mixture as in (*a*) did not alter the yield. Hydrogenation in pyridine containing palladised barium sulphate gave 38% of partly racemised phenol, $[\alpha]_D$ +23·5° in chloroform.

*l*-Dihydrorotenone gave a Goodhue value of 111, but rotenonic acid gave no colour in the test. Both substances gave a blue colour in the Durham test.

dl-iso*Rotenone.*—After *l*-*iso*rotenone (10 g.) and potassium carbonate (25 g.) had been heated under reflux in acetone (100 c.c.) for 2 hours, the mixture was poured into water; the precipitate, crystallised from alcohol, gave pure *dl*-*iso*rotenone (8·7 g.), m. p. 169—171°, α 0. The product gave the known inactive oxime, crystallising from alcohol in leaflets, m. p. 230° (cf. Takei, *Ber.*, 1928, **61**, 1003). *l*-*iso*Rotenone (1 g.) was partly racemised by heating in pyridine (5 c.c.) for 1 hour on the water-bath; the product had $[\alpha]_D$ −32·5° in benzene.

The oxime of *l*-*iso*rotenone was obtained by us only as an amorphous powder; it separated as a gel from quite dilute or concentrated solutions in alcohol, benzene, carbon tetrachloride, etc. Rotenoneoxime was readily obtained with m. p. 240—241°, $[\alpha]_D$ +134° in acetone, +37·5° in benzene; the dextrorotation is remarkable.

*Other Racemisations.*—After *l*-dihydrodeguelin (10 mg.), m. p. 155—156°, and anhydrous sodinm acetate (10 mg.) had been boiled in absolute alcohol (3 c.c.) under reflux for ½ hour, the solution, when cold, deposited *dl*-dihydrodeguelin, which, after washing with warm water to remove acetate, melted at 172° alone and at 173—174° when mixed with an authentic specimen, m. p. 175—176°.

A similar experiment with *l*-rotenonic acid (10 mg.), m. p. 208°, gave *dl*-rotenonic acid, which after crystallisation from benzene–ligroin melted at 183° and at 184° when mixed with an authentic specimen.

The feasability of doing such racemisations on a micro-scale is thus demonstrated.

*Acetyl*-dl-*isorotenone.*—(*a*) *l*-*iso*Rotenone (2 g.) and anhydrous sodium acetate (1 g.) were boiled gently under reflux in acetic anhydride (40 c.c.) for 1 hour. The mixture was poured into water and stirred until most of the anhydride was destroyed. The gummy product, separated by decantation of the supernatant liquid and crystallised from alcohol, gave material, m. p. 124—126°, $[\alpha]_D$ about −3° in benzene, which was separated by fractional extraction with hot methyl alcohol into (i) a more soluble fraction (75%), consisting of the *dl*-acetate, needles, m. p. 146°, α 0 in acetone or benzene, and giving no colour in the Durham test, and (ii) a less soluble fraction, needles, m. p. 150—155°, α 0, which gave a blue colour in the Durham test and thus contained unacetylated but racemised *iso*rotenone. Acetylation for only ½ hour gave some of the *dl*-acetate, but after heating for 10 minutes no acetate could be isolated.

(*b*) *dl*-*iso*Rotenone (2 g.) similarly gave the acetate (1·06 g.), m. p. 146° alone or mixed with the acetate described in (*a*) (Found: C, 68·8; H, 5·5. Calc. for $C_{25}H_{24}O_7$: C, 68·8; H, 5·5%), and a less soluble fraction which gave the Durham test.

Acetyl-*dl*-*iso*rotenone (1·75 g.) was boiled for 2 hours with alcohol (85 c.c.) and concentrated hydrochloric acid (15 c.c.). The product, isolated by pouring the mixture into water and filtering, was crystallised from the least amount of alcohol; it gave a 72% yield of *dl*-*iso*rotenone, m. p. 167°; a second crystallisation gave material m. p. 170°, unchanged by admixture with an authentic specimen. This experiment was done with identical results with the acetate prepared on one occasion from *l*- and on another from *dl*-*iso*rotenone.

*Acetylrotenone and its Hydrolysis.*—When preparing acetylrotenone (Cahn and Boam, *loc. cit.*), it is essential to dissolve the crude gummy product in at least 20 parts of hot alcohol and to start crystallisation by seeding and scratching; otherwise oils separate. Crystals for seeding are best obtained from more dilute solution. After attempted hydrolysis by very dilute acid, acetylrotenone was recovered in a *form*, m. p. 159—160° (Found: C, 68·8; H, 5·75. $C_{25}H_{24}O_7$ requires C, 68·8; H, 5·5%); thereafter, this form was obtained by acetylation of rotenone. The known form, m. p. 137°, for which we found $[\alpha]_D$ −172·5° in benzene, yields the new form when crystallised from alcohol and seeded with the latter, but the reverse change could not be effected.

Acetylrotenone (10 g.) was hydrolysed by boiling for 1 hour in alcohol (425 c.c.) and concentrated hydrochloric acid (75 c.c.). The precipitate obtained by pouring the reaction mixture into water gave, when crystallised from alcohol, 6·3 g. of rotenone, $[\alpha]_D$ −228° in benzene, m. p. 161—162° alone and 162—163° when mixed with an authentic specimen. Evaporation of the alcoholic mother-liquor and dissolution of the residue in carbon tetrachloride gave 1·75 g. of rotenone–carbon tetrachloride solvate (equivalent to 1·25 g. of rotenone), which was identified by conversion by alcohol into rotenone, the authenticity of which was confirmed in the way just described. Total yield, 83%.

β-*Toxicarol.*—Ordinary (α-)toxicarol (5 g.) and anhydrous potassium carbonate (10 g.) were heated under reflux in acetone (100 c.c.) for 2 hours. The mixture was then treated with water, acidified, and extracted with ether. The ethereal layer, kept overnight, deposited α-toxicarol (1·4 g.), which was removed by filtration and identified by crystallisation from acetic acid (m. p. and mixed m. p. 226°). The residue obtained by evaporating the filtrate was triturated with alcohol; a solid (3 g.), m. p. 155—160°, separated; several crystallisations of this from alcohol yielded pure β-*toxicarol* (2·1 g.) in pale yellow plates, m. p. 165—167° (Found: C, 67·4; H, 5·1 $C_{23}H_{22}O_7$ requires C, 67·3; H, 5·4%). Our product had a Goodhue value of 88; the deficiency below 100 may have been due to a content of α-toxicarol, but we have never obtained a higher value for β-toxicarol and so believe that given to be correct. In this connexion it is noteworthy that *l*-dihydrorotenone gave a Goodhue value over 100. In the Durham test β-toxicarol gives a blue colour, fading through pale green to yellow; this is quite distinct from the deep green colour given immediately by α-toxicarol.

When β-toxicarol (0·25 g.) and anhydrous sodium acetate (0·2 g.) in acetic anhydride (10 c.c.) were gently boiled under reflux for 20 minutes, the product (0·1 g.), isolated by pouring the

reaction mixture into water and crystallising the precipitate from acetic acid, had m. p. 220—223° and did not depress the m. p. of diacetyl-α-toxicarol. This tranformation indicates ring-fission by acetic anhydride. However, in a similar experiment with 2 g. of β-toxicarol we obtained material (1 g.), which melted at 180—190° and seemed from analyses to contain about 1·5 acetyl groups, but was unchanged by further acetylation. Acetylation for 6·5 hours gave a similar product. No definitely homogeneous product could be obtained by acetic anhydride in pyridine. It is possible that acetylation of β-toxicarol is sterically hindered, for that of the α-isomeride is a very smooth reaction, in which apparently no ring fission occurs.

*Effect of Alkali on β-Toxicarol.*—(*a*) β-Toxicarol (1 g.) and potassium carbonate (2 g.) in acetone (20 c.c.) were heated under reflux for 1 hour. The reaction mixture was poured into water, acidified, and shaken with ether. The ethereal layer, kept overnight, deposited α-toxicarol (0·2 g.), m. p. 220—223° (mixed m. p.). Evaporation of the filtrate gave a gum, from which trituration with alcohol separated β-toxicarol (0·6 g.), m. p. 155—160°, raised to 163—166° (alone or mixed with an authentic specimen) by recrystallisation from alcohol.

(*b*) β-Toxicarol (0·5 g.) in alcohol (10 c.c.) and 10% aqueous sodium hydroxide (0·2 c.c.) was boiled for 10 minutes. The solution, when cold, had deposited crude α-toxicarol (0·3 g.), m. p. 197—203°, just as in the preparation of toxicarol from a *Derris* extract; recrystallisation from acetic acid raised the m. p. to 227—229°, alone or mixed with an authentic specimen. The alcoholic mother-liquors, poured into water and worked up as in (*a*), gave 0·1 g. of red crystals, m. p. 180—185°.

(*c*) The mixture obtained by boiling β-toxicarol (1 g.) and anhydrous sodium acetate (3 g.) in alcohol (30 c.c.) was worked up as in (*a*) and gave 0·75 g. of crude α-toxicarol, m. p. 210—212°.

*Dehydro-β-toxicarol.*—Iodine (1 g.) in a little alcohol was added gradually to a boiling solution of β-toxicarol (1 g.) and anhydrous sodium acetate (3 g.) in alcohol (30 c.c.). After being boiled for a further 1 hour, the mixture was poured into water. The solid iodo-compound precipitated was collected, dried on porous tile, and reduced with zinc dust (2·5 g.) in boiling acetic acid for 2 hours, further zinc dust (1 g). being added at the end of the first hour. The hot solution was filtered from the zinc, which was washed with hot acetic acid. The filtrate and washings, poured into water, yielded *dehydro-β-toxicarol*, which crystallised from alcohol in minute yellow needles (0·6 g.), m. p. 180—184°, raised to 183—184° by further crystallisation by adding hot methyl alcohol to its solution in a little chloroform. In a similar experiment, in which, however, 2 c.c. of acetic acid were added before the iodine, we obtained 0·6 g. of the dehydro-compound, m. p. 183—188°. Three specimens were analysed, but, although we believe them to have been pure, gave low values for carbon (Found: C, 66·5, 66·9, 66·7; H, 5·0, 4·8, 4·9. $C_{23}H_{20}O_7$ requires C, 67·6; H, 4·9%); similar difficulty was met with dehydrodihydro-β-toxicarol. The structure was confirmed by acetylation.

The *acetyl* derivative, prepared by boiling the dehydro-compound (0·25 g.) and anhydrous sodium acetate (0·2 g.) in acetic anhydride (10 c.c.) for 10 minutes and pouring the resulting mixture into water, was obtained after several crystallisations from alcohol as colourless crystals (0·2 g.), m. p. 196—197° (Found: C, 66·4; H, 4·9. $C_{25}H_{22}O_8$ requires C, 66·5; H, 4·9%).

*Dihydro-β- and -α-toxicarol.*—β-Toxicarol (2 g.) and an Adams's platinum catalyst (0·3 g.) in "purified" dioxan (50 c.c.) were stirred under hydrogen until absorption was complete. The dioxan also absorbed hydrogen in the presence of this catalyst (but not of palladised barium sulphate), so that absorption was not measured. *Dihydro-β-toxicarol*, isolated from the filtered solution by precipitation by water, crystallised from alcohol–benzene in long, colourless needles (1·8 g.), m. p. 213—215° (Found: C, 66·7; H, 5·4. $C_{23}H_{24}O_7$ requires C, 67·0; H, 5·9%).

Dihydro-α-toxicarol was similarly obtained from α-toxicarol in 80—90% yield as colourless prisms, m. p. 206—207°. α-Toxicarol could not be hydrogenated when palladised barium sulphate was used in dioxan or hot or cold acetic acid.

Both dihydro-compounds give a blue colour in the Durham test.

*Dehydrodihydro-β-toxicarol.*—This *substance* was prepared from dihydro-β-toxicarol (1 g.), iodine (1·4 g.), and sodium acetate (3 g.) in absolute alcohol (100 c.c.) in the way described for dehydro-β-toxicarol, except that, owing to ready crystallisation, it was more convenient to decant the acetic acid solution from the zinc dust than to filter. Yellow leaflets, m. p. 226—227°, were obtained from chloroform–alcohol. Yield, 70%. Two preparations, believed to be pure, gave erroneous figures for carbon (Found: C, 68·3, 66·3; H, 5·3, 5·0. $C_{23}H_{22}O_7$ requires C, 67·3; H, 5·4%) (cf. dehydro-β-toxicarol). The *acetyl* derivative, prepared in the usual way, formed pale yellow needles, m. p. 175—176°, from alcohol and gave correct analytical figures (Found: C, 66·5; H, 5·6. $C_{25}H_{24}O_8$ requires C, 66·4; H, 5·3%).

*Dihydrotoxicarolic Acid.*—50% Aqueous potassium hydroxide solution (4·2 c.c.) was added to

dehydrodihydro-β-toxicarol (0·7 g.) and zinc dust (0·7 g.) in alcohol (17·5 c.c.), and the mixture heated for ½ hour under reflux. By working as described by Clark (*J. Amer. Chem. Soc.*, 1932, **54**, 2546), we obtained a 64% yield of dihydrotoxicarolic acid. This separated from aqueous methyl alcohol, as described, in colourless plates, m. p. 123—125° (decomp.), which, contrary to Clark, we found to contain two molecules of water of crystallisation (Found: C, 57·25; H, 6·2. $C_{23}H_{26}O_9,2H_2O$ requires C, 57·25; H, 6·3%. Calc. for $C_{23}H_{26}O_9$: C, 61·9; H, 5·9%). The acid, m. p. 125—128° (decomp.), prepared similarly from dehydrodihydro-α-toxicarol in 70% yield, was also the dihydrate (Found: C, 57·4; H, 6·45%). Neither specimen gave with aqueous or alcoholic ferric chloride the purple colour described by Clark; both gave, however, the methyl ester, colourless leaflets from aqueous methyl alcohol, m. p. 174—176°, and methyl ester diacetate, colourless needles from methyl alcohol, m. p. 143°. (For substances prepared in the β-series: ester: Found: C, 62·3; H, 6·3. Calc. for $C_{24}H_{28}O_9$: C, 62·6; H, 6·1%. Diacetate: Found: C, 61·9; H, 6·2. Calc. for $C_{28}H_{32}O_{11}$: C, 61·7; H, 5·9%.) The acids and their derivatives from the α- and the β-series gave no depressions of the melting points when appropriately mixed.

*Hydrolysis of Diacetyltoxicarol.*—Diacetyltoxicarol (2 g.), alcohol (100 c.c.), and concentrated hydrochloric acid (5 c.c.) were heated under reflux for 1 hour, poured into water, and shaken with ether. When kept overnight, the ethereal solution deposited *dl*-α-toxicarol, m. p. 225°, in quantitative yield.

*Acetylsumatrol.*—Sumatrol (0·5 g.) and anhydrous sodium acetate (1 g.) in acetic anhydride (5 c.c.) were gently boiled under reflux for 10 minutes. The mixture was poured into water and stirred until most of the anhydride was destroyed. Two crystallisations of the oily residue from alcohol afforded *acetylsumatrol* in long colourless needles, m. p. 218—219°, $[\alpha]_D$ −57·5° in benzene, −20·5° in acetone (Found: C, 66·3; H, 5·4. $C_{25}H_{24}O_8$ requires C, 66·3; H, 5·35%).

Hydrolysis by 5% alcoholic hydrochloric acid gave sumatrol, $[\alpha]_D$ −180° in benzene, m. p. 195° alone or mixed with an authentic specimen, in excellent yield.

l-α-*Toxicarol.*—(*a*) *Direct isolation from an extract.* In order to obtain *l*-α-toxicarol from a commercial *Derris* extract by ethyl acetate, we found it essential first to remove interfering substances. Addition of light petroleum (b. p. 40—60°) in small portions to a Sumatra-type extract in a little benzene precipitated first very discoloured fractions, which were discarded. When the precipitated gum had only a pale yellow colour, a large volume of light petroleum was added to precipitate the remainder of the insoluble matter. This left the waxy or fatty substances in solution and these too were discarded. The light-coloured precipitates were dissolved in a little ethyl acetate and treated with alcohol until, on seeding liberally and scratching, slow crystallisation began. After being kept overnight, the crystals were collected and recrystallised a few times from ethyl acetate–alcohol or ethyl acetate alone. As thus obtained, crude *l*-α-toxicarol had m. p. 100—101°, $[\alpha]_D$ about −65° to −70° in benzene and +46° in acetone, and was very soluble in cold acetone, ethyl acetate, acetic acid, benzene, chloroform, or carbon tetrachloride, hot ether, ethyl or methyl alcohol, and, which is unusual for this series, moderately soluble in hot light petroleum. Its rotation and melting point were not materially changed by further crystallisation. Further purification is described in (*d*) below.

(*b*) The following method is the counterpart to the above, but using alkali. It is essential for good yields that contact of the alkaline and ethereal solutions should be reduced to a minimum, and, particularly if emulsification occurs, portions of the solution should be sacrificed to speed of working; otherwise oxidation and partial racemisation occur. We shall refer to a solution of 50 g. of potassium hydroxide and 250 g. of potassium chloride in 1 l. of water as the "alkaline solution." A Sumatra-type extract (100 g.) in ether (500 c.c.) was shaken with two 20 c.c. portions of the "alkaline solution" and the precipitated dark brown, oily sludges were discarded (this is essential for ease of crystallisation later). The ethereal solution was then shaken with 150 c.c. of the "alkaline solution" and decanted from the yellowish sludge. This sludge was washed once or twice with ether and then acidified. The precipitated gum was taken up in ether and the whole process was repeated to effect further cleaning and to remove entangled non-phenolic material. The phenols were finally recovered from the ether and crystallised from ethyl acetate–alcohol as described in (*a*); crystallisation was made considerably easier by the use of alkali as just described. Both methods gave substances of similar properties and the following crystallo-optical description applies to both; though not absolutely complete, it is ample to establish identity.

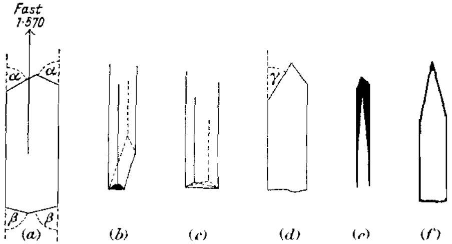
The substance separated from a mixture of equal parts of alcohol and ethyl acetate in pale pistachio green, bladed needles, most often arranged in radiating aggregates. A very characteristic form is shown in Fig. 5*a*. Different terminations, shown in Figs. 5*b*, *c*, and *d*, were common.

The needles almost always showed different terminations at opposite ends (Fig. 5*a*). Even the largest seen (0·03 mm. long) were practically non-pleochroic. Extinction was straight, the length direction fast, and the directions image in specimens as in Fig. 5*a* was either a large obtuse axial angle or else the "flash figure" of the normal to the optic axial plane. The double refraction was moderate and $n_D$ along the length was 1·570 ± 0·003. Forms shown in Figs. 5*e* and *f* were common in some recrystallisations. Angles measured were: α 61 ± 1°, β 79 ± 1°, γ 36 ± 3°.

(*c*) The following method is the simplest and gives the best yield. A Sumatra-type extract (200 g.) in ether (1 l.) was well shaken in a succession of flat-bottomed flasks with successive portions of the "alkaline solution" until no more precipitation of potassum salts occurred (there is no need to discard the early precipitates in this case); the ethereal layer was on each occasion readily decanted from the aqueous alkaline sludge. These sludges were washed individually by shaking with ether, separated by decantation, united, and acidified; the precipitated phenols were removed in a large volume of ether. Solid material (*A*) separated and was removed after 36 hours; this (10—12 g.) was a complex mixture, from which fractional extraction with alcohol removed first crude sumatrol, m. p. 175—180°, and then high-melting products, which were probably dehydro-compounds but may have contained some *dl*-α-toxicarol.

FIG. 5.

*Crude* l-α-*toxicarol*, $[\alpha]_D$ *about* −68° *in benzene, about* +50° *in acetone; crystallised from* 1 : 1 *ethyl acetate–alcohol.*



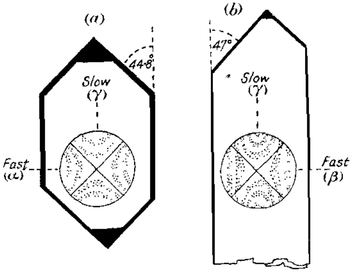

The ethereal filtrate from (*A*) was dried over sodium sulphate, concentrated to about 250 c.c., seeded, and kept for 10 days, during which time a crumpled, twisted mass of compacted, nodular aggregates of small needles separated. This (74 g.) was broken up, collected, and washed with ether, and then had m. p. 101°, $[\alpha]_D$ +50° in acetone. A gum obtained from the ethereal filtrate by evaporation gave a further 16 g. of impure *l*-α-toxicarol by the ethyl acetate–alcohol method. The material recovered from these final mother-liquors was extracted from ether by the "alkaline solution," this treatment being repeated several times; a final crop of 6 g. of crude *l*-α-toxicarol was thus obtained.

(*d*) *Purification.* Repeated recrystallisation of the products obtained by any of the above methods gave material having constant $[\alpha]_D$ +50° in acetone, +68° in benzene, and a constant m. p. about 101—102°. All the preparations, however, yielded to the following treatment. It is advisable to use batches of not more than 5 g. for the early operations, but to have at least 20 g. in all of material available. The crystals obtained from ethyl acetate were triturated with not too much ether; a small amount of colourless sumatrol remained behind; the amount of ether to be taken is best judged by the fact that the undissolved crystals are pure white. Concentration of the ethereal filtrate gave crystals, which were converted by crystallisation from ethyl acetate into purer material (*A*). The ethyl acetate mother-liquors were diluted with about 10 volumes of alcohol and shaken with water and ether (the alcohol assists removal of the ethyl acetate, which is essential); concentration of this ethereal solution gave crystals, from which trituration with a little fresh ether (*B*) separated a further quantity of sumatrol. Concentration of the ethereal filtrate (*B*) therefrom gave crystals (*A*′). Crystals (*A*) and (*A*′) were united and crystallised alternately from ether and ethyl acetate until they reached constant [α]. Ethyl acetate mother-liquors were treated as just described (alcohol, water, ether, etc.); ethereal mother-liquors were concentrated to give fresh crops. All crystals obtained from

mother-liquors were triturated with ether; when, with the purer specimens, this failed to separate sumatrol, they were crystallised alternately from ethyl acetate and ether. [α] was determined for each crop, and similar crops and similar mother-liquors were combined. In this way the bulk of the material was separated into sumatrol and pure *l-α-toxicarol*, m. p. 101—102°, $[\alpha]_D$ −53° in benzene, +69° in acetone (Found in different preparations: C, 67·3, 67·2; H, 5·9, 5·9. $C_{23}H_{22}O_7$ requires C, 67·3; H, 5·4%). The crude sumatrol obtained had m. p. about 180°; it was very readily purified by recrystallisation, probably best from acetone–alcohol or ethyl acetate, to give material, m. p. 189°. It is known to crystallise without solvent of crystallisation from alcohol and was found to do so also from ethyl acetate (Found: C, 67·65; H, 5·4. Calc. for $C_{23}H_{22}O_7$: C, 67·3; H, 5·4%).

FIG. 6.

*Pure* l-α-*toxicarol, m. p.* 127°, *crystallised from alcohol.*



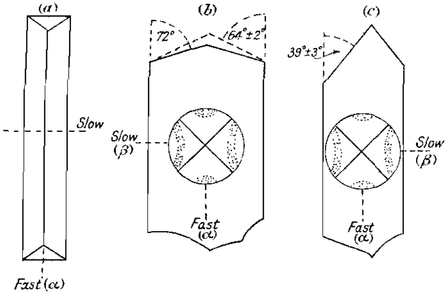

(a) *Very common form of tabular crystal, lying so as to show directions image normal to the optic axial plane.* (b) *Crystal lying on edge, to show the emergence of the acute bisectrix,* 2V *large, negative.*

Well-defined crystals are obtained from ethyl acetate solutions of *l*-α-toxicarol, $[\alpha]_D$ +50° in acetone, but from ether or light petroleum only if $[\alpha]_D$ > +60° in acetone. When pure, the substance forms beautiful canary-yellow needles, m. p. 101—102° (capillary tube), from ethyl acetate, ether, or ethyl acetate. From alcohol or light petroleum we got a *form*, m. p. 126—127° (Found: C, 67·3; H, 5·3. $C_{23}H_{22}O_7$ requires C, 67·3; H, 5·4%).

As observed under the microscope, *l*-α-toxicarol crystallises from alcohol fairly easily in pale green, tabular crystals, m. p. 127°, having the characteristic forms shown in Fig. 6*a* and *b*.

FIG. 7.

*Pure* l-α-*toxicarol, m. p.* 102°, *crystallised from ethyl acetate.*




(*a*) *Common needle form.* (b) *and* (c) *Common plate forms; the variation in the angular values is in part due to the crystals being tilted slightly. The dotted termination in* (b) *shows another common end form. A bisectrix, probably that of the obtuse angle, emerges normal to the plate.*

Straight extinction is always given parallel to the length, which is the direction of slow vibration γ. $n_D$ are α 1·551, β 1·664, γ 1·742 (all ±0·003). The common form (Fig. 7*a*) presents a section normal to the optic axial plane and gives α and γ. Some crystals lie at right angles to this (Fig. 6*b*) and give a large acute bisectrix directions image of negative character; these give β and γ. The optic axial angle is large, 2*V* being about 75°.

The form, m. p. 103—104° (on a warm stage), is quite distinct from that, m. p. 127°. It presents two habits: fine needles of the type shown in Fig. 7*a*, and plates, characteristic forms

of which are shown in Figs. 7*b* and *c*. The colour is very faint yellowish-green, and the fast direction is along the length of the needles and elongated plates. $n_D$ are α 1·570, β 1·645, γ 1·679 (all ±0·003). All sections presented by plates and needles give straight extinction. The characteristic directions image given on the broad face of the plates is shown in Fig. 7*b*. It was difficult to measure γ across the edges of the plates and this value may not be so accurately determined as the others.

(*e*) The experiments described in (*a*)—(*c*) were done with extract containing 4% of rotenone and giving a ferric chloride value of 60. Two other extracts were treated by method (*b*). One, containing 2% of rotenone and giving a ferric chloride value of 68, gave material, which by repeated crystallisation was obtained with m. p. 102°, $[\alpha]_D$ +54° in acetone; treatment by method (*d*) separated sumatrol from these crystals. The other extract, containing 6% of rotenone and giving a ferric chloride value of 53, gave by the same methods a material, m. p. 102—102·5°, $[\alpha]_D$ +59° in acetone, from which also a little sumatrol was obtained by method (*d*). These additional extracts were chosen as representative of the two extremes of Sumatra-type extracts. It is plain that the occurrence of sumatrol and the difficulty of separating it from *l*-α-toxicarol are general, but it seems that simple crystallisation gives finally a material which differs slightly from case to case; the formation of a true molecular compound seems to be excluded.

(*f*) A normal *Derris* extract (100 g.), containing 28% of rotenone and giving Goodhue and ferric chloride values of 49 and 13, respectively, in ether (1 l.) was shaken with an excess of the "alkaline solution." The precipitate formed in the aqueous layer (which assumed a deep brown colour) was collected by filtration and treated with dilute acid and ether. Evaporation of the ethereal layer gave a residue, which was dissolved in ethyl acetate (about 10 c.c.), treated with alcohol (about 100 c.c.), seeded, and kept overnight. The yellowish crystalline sludge (2 g.), which had separated, was collected and triturated with cold ether, whereby a mixed insoluble residue was obtained; concentration of the ethereal filtrate gave, after cooling, crystals, from which by trituration with ether 0·15 g. of sumatrol, m. p. 178—181°, was isolated. The sumatrol, when recrystallised, had $[\alpha]_D$ −175° in benzene and m. p. 188° alone or mixed with an authentic specimen. The final ethereal mother-liquors gave by concentration impure *l*-α-toxicarol, m. p. 100°, $[\alpha]_D$ +60° in acetone. N.B. This experiment has qualitative, but not quantitative, significance.

(*g*) Acetylation of *l*-α-toxicarol was not a smooth process, no matter what the degree of purity of the material, and results were not reproducible. Material, $[\alpha]_D$ +50° in acetone, gave in various experiments small amounts of acetylsumatrol, m. p. 217°, $[\alpha]_D$ −56·5° in benzene, hydrolysed by acid to sumatrol of correct [α] and m. p. (mixed m. p.), and/or more soluble, colourless prisms, m. p. 158°, $[\alpha]_D$ +70° in acetone, separable by fractional extraction with hot alcohol. Neither acetate gave a ferric chloride colour, so that in both it is the phenolic hydroxyl group which is acetylated. The prisms appear to be *monoacetyl*-l-*α-toxicarol* (Found: C, 66·0; H, 5·2; $CH_3$·CO, 11·7. $C_{23}H_{21}O_7$·CO·$CH_3$ requires C, 66·3; H, 5·35; $CH_3$·CO, 9·7%), for the same product was obtained in some experiments in poor yield from pure *l*-α-toxicarol and it gave on hydrolysis by dilute alcoholic hydrochloric acid a substance, m. p. 98—101°, which did not depress the m. p. of pure *l*-α-toxicarol. We are unable to assert categorically—although it seems inevitable—the structure of this acetyl derivative, as we had insufficient material to determine [α] of the regenerated phenol. The difficulty of acetylating *l*-α-toxicarol may be due to racemisation and is paralleled by the behaviour of β-toxicarol, but is in marked contrast to the smooth acetylation of *dl*-α-toxicarol. In this connexion the acetylation of *l*-dihydro-α-toxicarol to *dl*-diacetyldihydro-α-toxicarol, described below, should be noted.

*Equilibration of* l-*α-Toxicarol*.—(*a*) To *l*-α-toxicarol (0·5 g.; $[\alpha]_D$ +68° in acetone) in benzene (10 c.c.) was added 1·7% methyl-alcoholic potassium hydroxide solution (4 c.c.; 1 equiv.) and thereafter within 10 seconds an excess of acetic acid. The solution was washed with water, dried, and evaporated. The residue, crystallised from alcohol, gave *l*-α-toxicarol (0·27 g.), $[\alpha]_D$ +67° in acetone, m. p. 126—128° alone or mixed with an authentic specimen.

In a similar experiment, in which, however, no acid was added, the following rotations were observed when the solution was kept:

| Time, mins. ......... | < 0·5 | 2 | 5 | 10 | 15 | 30 | 120 | 300 | 1440 |
|---|---|---|---|---|---|---|---|---|---|
| $[\alpha]_D$ .................. | +350° | +280° | +224° | +193° | +171° | +140° | +70° | +46° | 0° |

A similar solution in benzene–methyl alcohol without alkali had $[\alpha]_D$ −46°. When worked up at the end of 24 hours, the inactive solution yielded *dl*-α-toxicarol (0·3 g.), m. p. 225—227° alone or mixed with an authentic specimen.

(*b*) 5% Aqueous potassium hydroxide solution (0·5 c.c.) was added to *l*-α-toxicarol (2 g.) in boiling alcohol (10 c.c.) and the whole was boiled for 10 minutes. The resulting rather

stiff paste was acidified with acetic acid and kept overnight. *dl*-α-Toxicarol (1·95 g.), m. p. 217—219° (mixed m. p.), was then collected in a Gooch crucible.

(*c*) *l*-α-Toxicarol (1 g.) and anhydrous sodium acetate (3 g.) in alcohol (25 c.c.) were heated under reflux for 2 hours The product, obtained by dilution with water and recrystallised, afforded *dl*-α-toxicarol (0·7 g.), m. p. 224° (mixed m. p.). In a similar experiment, in which, however, 2 c.c. of acetic acid were added to the boiling mixture, *dl*-α- (0·55 g.), m. p. 218° (mixed m. p.), and also *dl*-β-toxicarol (0·3 g.), m. p. 155° (mixed m. p.), were isolated. For separation of the two isomerides in this and similar experiments, see the preparation of β-toxicarol.

(*d*) 1% Methyl-alcoholic potassium hydroxide solution (3 c.c.) was added to *l*-α-toxicarol (2·5 g.) in acetone (50 c.c.). After 48 hours *dl*-α-toxicarol (0·9 g.) had separated. The filtrate therefrom yielded *dl*-β-toxicarol (0·85 g.).

(*e*) *l*-α-Toxicarol (1 g.) and anhydrous potassium carbonate (2 g.) in acetone (20 c.c.) were heated under reflux for 2 hours. The mixture, poured into water, gave *dl*-α- (0·4 g.) and *dl*-β-toxicarol (0·45 g.).

(*f*) When *l*-α-toxicarol (3 g.) in ether (50 c.c.) was shaken with an excess of 3% aqneous barium hydroxide, a bright yellow, insoluble barium salt was precipitated. This was soluble in acetone, but sparingly so in alcohol. The salt, washed successively with water and ether, was boiled in suspension in alcohol (150 c.c.) for 10—15 minutes. The mixture, acidified with acetic acid, gave *dl*-α-toxicarol (2 g.).

*Dehydrogenation of* l-α-*Toxicarol.*—Iodine (1·2 g.) in a little alcohol was added gradually to *l*-α-toxicarol (1 g.) and anhydrous sodium acetate (3 g.) in boiling alcohol (25 c.c.), and boiling was continued for a further 2 hours. Further working proceeded as described for dehydro-β-toxicarol. The product crystallised from chloroform–methyl alcohol in pale yellow needles, α 0, m. p. 228—230° alone or mixed with dehydro-α-toxicarol (m. p. 229—231°).

*Dihydro*-l-α-*toxicarol.*—*l*-α-Toxicarol (4 g.) and a platinum oxide catalyst (0·25 g.) in "purified" dioxan (50 c.c.) were stirred under hydrogen until absorption ceased. l-*Dihydro*-α-*toxicarol*, isolated by pouring the filtered mixture into water and crystallising the product from alcohol, formed colourless needles (2·6 g.), m. p. 178—180°, $[\alpha]_D$ −57° in benzene (Found: C, 67·5; H, 5·85. $C_{23}H_{24}O_7$ requires C, 67·0; H, 5·9%). Further crystallisation did not affect these constants. This substance crystallises very readily and is easily obtained in good yield from quite crude *l*-α-toxicarol; so obtained, however, it is completely purified only with difficulty.

A similar experiment in acetic acid gave a better yield (85%).

When this substance (0·5 g.) and anhydrous sodium acetate (0·2 g.) in acetic anhydride (5 c.c.) were gently boiled under reflux for 10 minutes and then poured into water, tbe residue left after destruction of the anhydride crystallised from alcohol in colourless needles (0·3 g.), m. p. 184—186°, $[\alpha]_D$ +64·5° in acetone. This was the *monoacetate* of the active compound (Found: C, 66·1; H, 5·8; $CH_3$·CO, 9·7. $C_{23}H_{23}O_7$·CO·$CH_3$ requires C, 66·0; H, 5·8; $CH_3$·CO, 9·7%); the phenolic group is esterified, as the compound gives no colour with ferric chloride. Hydrolysis by hot 5% alcoholic hydrochloric acid for ½ hour gave the active parent phenol of unchanged rotation and m. p. (mixed m. p.). Heating for 2 hours in a similar acetylating experiment gave 0·12 g. of inactive diacetyldihydro-α-toxicarol, m. p. 226° alone or mixed with an authentic specimen.

When 1·7% methyl-alcoholic potassium hydroxide (4 c.c.) was added to (*A*) *l*-dihydro-α-toxicarol or (*B*) its acetate (0·5 g.) in benzene (10 c.c.) and kept, the following rotations were observed:

| Time, mins. | < 0·5 | 2 | 5 | 10 | 30 | 60 | 120 | 240 | 360 | 1440 |
|---|---|---|---|---|---|---|---|---|---|---|
| (*A*) $[\alpha]_D$ ...... | +273° | +255° | +238° | +227° | +172° | +112° | +45·5° | +23·5° | +16° | 0° |
| (*B*) $[\alpha]_D$ ...... | +112° | + 72° | + 70° | — | — | + 30° | — | — | +17° | 0° |

This confirms the structure assigned to the acetate by showing that the asymmetry of the C7—C8 centre is intact.

An attempt to isolate the products of racemisation of dihydro-*l*-α-toxicarol was nnsuccessful, probably because of the similar solubilities of the α- and β-dihydro-compounds.

Dehydrogenation of *l*-dihydro-α-toxicarol in the usual way gave dehydrodihydro-α-toxicarol, identified by the m. p. (258°) and mixed m. p. with an authentic specimen and by preparation from it of the acetyl derivative, m. p. 236° alone or mixed with an authentic specimen.

*Mutarotation of Sumatrol.*—Under the conditions described for *l*-dihydro-α-toxicarol, etc., the following rotations were observed for sumatrol:

| Time, mins. ......... | 1 | 2 | 5 | 10 | 60 | 120 | 210 | 360 | 1440 |
|---|---|---|---|---|---|---|---|---|---|
| $[\alpha]_D$ .................... | +105° | +84° | +59° | +49° | 0° | −33·5° | −42° | −43·5° | −42° |

$[\alpha]_D$ for a similar solution without alkali was −158°.

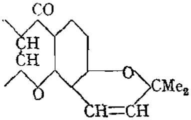
*Effect of Activated Alumina on* l-*α-Toxicarol*.—*l*-*α*-Toxicarol (1 g.; $[\alpha]_D$ +68° in acetone) in a little chloroform was run on to a column, 25 cm. long and 2 cm. in diameter, of B.D.H.'s "activated alumina for adsorption" (only the part retained on a 200 mesh sieve). The chromatogram was developed with chloroform until the canary-yellow zone extended down half the column; it was quite uniform. Soxhlet extraction with hot acetone–acetic acid, removal of the solvents, and dissolution of the residue in ether (5 c.c.) gave *dl*-*α*-toxicarol (0·06 g.), m. p. 217—219° (mixed m. p.). No other crystalline material could be isolated. A similar experiment in benzene gave 0·08 g. of *dl*-*α*-toxicarol as sole crystallisable product. In all experiments with activated alumina, elution of material from the column was extremely difficult. Merck's activated alumina gave similar results.

*Apotoxicarol*.—By Clark's method (*J. Amer. Chem. Soc.*, 1932, **54**, 2543) *dl*-and *l*-*α*-toxicarol gave the same (mixed m. p.) apotoxicarol, which after crystallisation from acetic acid–methyl alcohol had the recorded m. p., 246°, but contained a molecule of water of crystallisation unnoticed by Clark (Found in samples prepared from the *dl*- and the *l*-compound, respectively: C, 59·6, 58·8; H, 4·9, 4·9. $C_{18}H_{16}O_7,H_2O$ requires C, 59·3; H, 4·9%. Calc. for $C_{18}H_{16}O_7$: C, 62·5; H, 4·7%). Authenticity was confirmed by preparation of the triacetate, m. p. 206—207° (Clark gives m. p. 206°).

*Action of Sulphuric Acid on the Toxicarols*.—Concentrated sulphuric acid in acetic acid (cf. Wright, *loc. cit.*) transforms *l*- and *dl*-*α*- and β-toxicarol into substances, which crystallise with difficulty from chloroform–alcohol; these products are hard to purify owing to their sparing solubility and are hard to characterise, as they all melt above 300°. We do not know the nature of these substances, but record the following observations. All give green colours with alcoholic ferric chloride and in the Durham test. The product from *l*-*α*-toxicarol has $[\alpha]_D$ −208° in benzene and is racemised by alcoholic alkali. Dehydrogenation by iodine, etc., gives products, which are presumably dehydro-compounds, since they give no colour in the Durham test.

*Absorption Spectra*.—The determinations of absorption spectra were made on a Hilger $E_2$ quartz spectrograph used in conjunction with a "Spekker" photometer. The solvent used was (unless otherwise stated) ethyl alcohol specially purified until it was completely free from substances absorbing above 2200 A. Some absorption curves are shown in Fig. 2, and the exact locations of the absorption maxima, together with the intensities of absorption (as molecular extinction coefficients ε) at the maxima, are tabulated below. The determinations were made immediately after the preparation of the solutions, it having been found that several of the compounds deteriorated rapidly in alcohol (in 24 hours).

Our curve for rotenone is very similar to that reported by Seaber (*J. Soc. Chem. Ind.*, 1937, **56**, 168T). Seaber found the maximum at 2930—2940 A. (ours is at 2960 A.) and his $\varepsilon_{molar}$ is 18,400 (ours is 16,000). These differences are possibly due to difference in the solvent, Seaber having used *iso*propyl alcohol.




The absorption of sumatrol is very similar to that of rotenone. Deguelin, as shown in the annexed partial formula, bears the same relation to toxicarol as rotenone does to sumatrol, *i.e.*, it has the same structure in ring *E* but no hydroxyl group in ring *D*. The absorption of deguelin closely resembles that of toxicarol. We consider this as confirming the structure (XXII) assigned to sumatrol (cf. p. 522).

In both pairs, rotenone–sumatrol and deguelin–toxicarol, introduction of a phenolic hydroxyl group has intensified the absorption and displaced the principal maximum 20—35 A. towards the visible region; although these displacements are not a great deal larger than the experimental error, they are probably real, since they occur in both cases.

| | Wave-lengths of maxima in A. | Mol. extinct. coeff. ε. |
|---|---|---|
| Rotenone | 2960 | 16,000 |
| | 2370 | 14,400 |
| Sumatrol | 2980 | 23,000 |
| | (2350) | 16,600 |
| Deguelin | 2690 | 29,500 |
| | (3150) | 9,300 |
| Toxicarol | 2725 | 34,700 |
| | 2970 | 11,300 |
| Acetylrotenone | 3730 | 27,500 |
| | 3540 | 29,500 |
| | 2500 | 17,300 |

| | Wave-lengths of maxima in A. | Mol. extinct. coeff., ε. |
|---|---|---|
| Diacetyltoxicarol | 3775 | 25,800 |
| | 3590 | 27,600 |
| | 2960 | 15,500 |
| | 2580 | 25,400 |
| Dehydrorotenone | 3110 | 18,600 |
| | 2800 | 21,800 |
| | 2365 | 28,000 |
| M/20,000-Toxicarol in M/20-aqueous alcoholic NaOH | 2800 | 27,000 |

Comparison of diacetyltoxicarol with acetylrotenone shows a displacement of the main absorption maxima with the former substance 45—50 A. towards longer wave-lengths. In this case the extra hydroxyl group is masked. Both substances contain the conjugated system, aromatic ring *A*-C7 : C15-aromatic ring *D*. In diacetyltoxicarol the ethylenic linking of ring *E* is conjugated with ring *D* and so extends the system; it is possible that this accounts for the displacement. It is true that, by analogy with Kuhn's diphenylpolyenes, one might expect a much higher displacement (about 150 A.) for an additional ethylenic linking, but the structural analogy between these polyenes and substances of the rotenone series is far from close, and we believe the small positive displacement observed to be significant.

The maximum of absorption for toxicarol in aqueous alcoholic sodium hydroxide is not displaced by any means to the position of diacetyltoxicarol, as might be expected if complete enolisation took place. Complete, or nearly complete, enolisation is indicated by ns for toxicarol in benzene–methyl alcohol containing much potassium hydroxide, bnt our chemical work gives no indication of the quantitative extent of enolisation under other conditions. The displacement of the principal maximum of toxicarol from 2725 to 2800 A. in aqueous alcoholic sodium hydroxide is definitely significant of some enolisation. No displacement occurred with rotenone under these conditions.

We are indebted to Messrs. Cooper, McDougall and Robertson, Ltd., Berkhamsted, for permission to publish these results.

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## 107. *Aldol Condensation Products.*

By (Miss) Millicent M. T. Plant.

A study has been made of the water-soluble products obtainable from aldol by suitable condensation. An account is given of the preparation and reactions of these compounds and of their methyl and acetyl derivatives, for which structural formulæ have been deduced. It is suggested that the condensation occurring is of a simple aldol type, resulting in the formation of hydroxylated aldehydes which react as cyclic lactol forms.

Whilst a considerable amount of work has been carried out recently on the condensation of unsaturated aldehydes, in particular of crotonaldehyde, very little appears to have been accomplished in the parallel cases of the saturated hydroxylated compounds derived from aldol. The condensation of acetaldehyde to aldol in the presence of dilute alkali is well known, and a further condensation under similar conditions can easily be effected, one such process having been described by Raper (J., 1907, **91**, 1831), who also gives an account of a preliminary investigation of the condensation products.

In the experiments now to be described, the starting material was obtained by the condensation of crude aldol in concentrated aqueous solution by the addition of small quantities of lime, the reaction being allowed to proceed until compounds ranging roughly from $C_8$ to $C_{12}$ resulted. The product was a slightly viscid, yellow syrup, readily soluble in water or alcohol, insoluble in other organic solvents.

The aldol condensation product exerted a weakly reducing action, so the possibility of effecting a mild oxidation prior to a possible fractionation was investigated. This included oxidation by silver oxide, wherein silver deposits were formed but no silver salts could be isolated, and treatment with bromine water and aqueous potassium permanganate, there being in each case a rapid absorption of the reagent but no evidence for carboxylic compounds resulting. It was concluded that –CHO $\longrightarrow$ –CO·OH was not the primary reaction involved, but that the compounds were vulnerable to oxidative attack, possibly

at a double bond. In permanganate oxidation there was always an evolution of carbon dioxide, and the reaction appeared to be analogous to that given by the methyl derivatives shortly to be described, where the reaction of a carbonyl group is eliminated. This absence of true aldehydic function was borne out by the difficulty experienced in effecting condensation with the usual carbonyl reagents, *e.g.*, phenylhydrazines, from which no satisfactory products could be isolated.

By treatment of the crude aldol product at room temperature with dry methyl alcohol containing a trace of hydrogen chloride, methyl derivatives were readily formed, the viscid syrupy product resembling the original material in appearance and viscosity, but differing greatly in solubility, being almost insoluble in water, readily soluble in alcohol and other organic solvents. The compounds so obtained were non-reducing and stable to alkali, but were rapidly demethylated on treatment with dilute mineral acid. Methoxyl estimations on various samples indicated that methylation proceeded to some fixed point, roughly constant figures being obtainable, which corresponded to that required for half acetal formation on the assumed degree of polymerisation.

From the fact that the starting material was obtained from crude aldol containing unchanged acetaldehyde, under conditions essentially similar to those applied for the preparation of aldol itself, it seemed plausible to assume that the final products may be regarded as acetaldehyde condensation products, the condensation being of an aldol type to give a mixture of closely related polymers restricted to some definite range. In order that such a process may be repeated indefinitely condensation must proceed regularly as indicated,

$$CH_3\cdot CH(OH)\cdot CH_2\cdot CHO + CH_3\cdot CHO + CH_3\cdot CHO + \ldots \longrightarrow CH_3\cdot[CH(OH)\cdot CH_2]_n\cdot CHO$$

although the possibility of aldolisation of the active α-methylene group in the aldol is not excluded and would give rise to branched chain compounds, *e.g.*,

$$\begin{array}{c} CH_3\cdot CH(OH)\cdot CH_2\cdot CHO \\ CH_3\cdot CHO \end{array} \longrightarrow \begin{array}{c} CH_3\cdot CH(OH)\cdot CH\cdot CHO \\ CH_3\cdot CH\cdot OH \end{array} \longrightarrow \begin{array}{c} CH_3\cdot CH(OH)\cdot CH\cdot CH(OH)\cdot CH_2\cdot CHO, \text{ etc.} \\ CH_3\cdot CH\cdot OH \end{array}$$

For the various possibilities it is found that they have in common alternate hydroxylated carbon atoms, and in many cases there is a chain of six or more such carbon atoms terminated by an aldehyde group. From steric considerations, and by analogy with well-known cases of oxy-cyclo tautomerism in γ- and δ-hydroxy-aldehydes or -ketones, it seemed reasonable to suppose that these compounds should have a cyclic structure represented in the simplest case by

$$CH_3\cdot CH(OH)\cdot CH_2\cdot CH(OH)\cdot CH_2\cdot CHO \rightleftharpoons CH_3\cdot \overset{\lceil\quad\quad O \quad\quad\rceil}{CH\cdot CH_2\cdot CH(OH)\cdot CH_2\cdot CH}\cdot OH$$

Such a lactol ring structure seemed all the more probable in view of the modified aldehydic functions exhibited and the ready formation and stability of the methyl derivatives.

In order to obtain further insight into the constitution of these aldol products it was necessary first to isolate individuals from the supposed mixture of polymers. For this purpose a fractionation of the methyl derivatives seemed suitable, inasmuch as the molecule was thought to be stabilised by the presence of the lactol methyl group and it was hoped to use these compounds for the preparation of further derivatives. The crude methylated material was volatile at moderate temperatures and very low pressures, but a separation by fractional distillation was unsuccessful.

Pursuing a similar line of attack, it was thought that such compounds should be capable of further methylation to give methyl ether derivatives of the methyl-lactolides, to which the fractional distillation or other method for separation might then be applied. This also proved impracticable, since it was not possible to effect a further methylation of the crude methylated material or of the partly fractionated mixtures by the use of methyl iodide or methyl sulphate and alkali. On the other hand, by using either of these reagents

with the original aldol product, it was possible to obtain methyl derivatives similar to those prepared by use of methyl alcohol, though usually of slightly lower methoxyl content.

As an alternative to methylation, benzoylation of the methyl-lactolides was attempted but with no success.

This incapacity for further methylation, pointing to the absence of hydroxyl groups, might be accounted for by a dehydration similar to the aldol–crotonaldehyde conversion, so tests for ethenoid reactivity were applied. Potassium permanganate in acetone was rapidly decolorised and there was a measurable absorption of hydrogen with a platinum catalyst, though in neither case could satisfactory quantitative relationships be established; with perbenzoic acid there was no reaction. The course of the reaction with bromine in chloroform or carbon tetrachloride solution suggested that substitution as well as addition had occurred. The evidence for unsaturation was inconclusive, an interpretation of the results being very considerably complicated by the fact that the fractionated products investigated were undoubtedly mixtures.

On the other hand there was definite evidence forthcoming for the presence of potential hydroxyl groups, in the possibility of acetylatiou, which gave rise to products separable by distillation into well-defined fractions. Preliminary experiments on the acetylation of the free aldol material under mild conditions had shown little promise, but derivatives of the methyl-lactolides were readily prepared by treatment with acetic anhydride at its boiling point. Moreover, it is perhaps significant that at lower temperatures reaction did not appear to proceed to any extent, even when the reactants were heated together for a considerable time, whereas under the conditions applied, reaction occurred rapidly and with considerable evolution of heat. The crude products so obtained were reddish-brown syrups, rather more mobile than the untreated material, and still retained the methyl-lactolide group intact.

This mixture of acetates was submitted to a fractional distillation at low pressures, a separation into sharply defined fractions being attainable after three distillations, the b. p. of the products being 15—20° lower than those of supposedly corresponding methyl-lactolides. They were readily distinguishable from the latter by the greater mobility of the lower fractions and their pleasant, ester-like smell, which showed an increased tendency to pungency in the more viscid, higher fractions. The two lowest fractions were taken for further investigation, as described in the experimental section, these being obtained in 10% and 20% yields, and from their physical constants were considered to be chemical individuals. Considerable difficulty was encountered in obtaining satisfactory analytical figures for these products in spite of their apparent purity, so notes on the nature of the difficulties and the special procedure adopted have been included.

The experimental findings show that the behaviour of aldol condensation products is unexpectedly complicated, so it is difficult to assign structural formulæ to the various derivatives obtained. A study of the methylated derivatives and their acetates renders their formulation as cyclic lactolides highly probable. From the behaviour of the more volatile acetate isolated (*acetate* I) and the analytical figures obtainable from it, it seems probable that it is derived from the lactol form of the simple linear condensation product of three molecules of acetaldehyde and that it may be represented by the structure $CH_3{\cdot}CH{\cdot}CH_2{\cdot}CH(OAc){\cdot}CH_2{\cdot}CH{\cdot}O{\cdot}CH_3$ (ring: └——O——┘ linking the first CH and the last CH). The second acetate isolated (*acetate* II) is thought to be derived from a higher polymer, resulting from the condensation of four molecules of acetaldehyde, and to have the structure

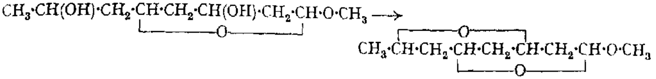
$$CH_3{\cdot}CH(OAc){\cdot}CH_2{\cdot}CH{\cdot}CH_2{\cdot}CH(OAc){\cdot}CH_2{\cdot}CH{\cdot}O{\cdot}CH_3,$$

└——O——┘

which is in agreement with its chemical behaviour and the analyses obtainable from it.

In view of the impossibility of fractionating the methyl aldols completely, suggestions for their structure are more tentative, though by their close relationship to the acetates a corresponding formulation as methyl-lactolides of polyhydroxy-aldehydes is possible. To account for the apparent absence of hydroxyl groups and of definite unsaturation, it

is thought that for the higher homologues dehydration with the formation of an anhydro-ring may have occurred, *e.g.*,



Acetylation would then be preceded by a fissure of the anhydro-ring, thus accounting for the vigorous conditions necessary and the course of the reaction with acetic anhydride.

## EXPERIMENTAL.

*Preparation of Aldol Condensation Products.*—Aldol (100 g.), dissolved in an equal weight of water, was treated with lime (2 g.), added to the well-stirred mixture during 30 minutes. The reaction was carried out at room temperature, though there was an initial rise of 5° with a simultaneous development of yellow coloration and increase in viscosity. Stirring was continued for 3—4 hours; the titration figure for a small aliquot portion, treated with hydroxylamine hydrochloride for estimation of carbonyl group, had then decreased to one-third of its original value, this being taken as a rough index of the degree of condensation which had occurred. Lime was removed by precipitation as calcium carbonate, resinous material was extracted with chloroform, and the remaining aqueous solution was evaporated at 50°/20 mm., small quantities of side products, thought to be calcium salts, being precipitated by addition of acetone when the solution had been partly concentrated. The product was a slightly viscid, yellow syrup with an aldol-like smell, soluble in water and alcohol, very sparingly soluble in ether and other organic solvents. By heating in a stream of dry air for several hours at 45°/20 mm. there was a loss in weight of approximately 12%, the carbonyl figure being simultaneously reduced from 10·5% to 7·5%. This was accounted for by supposing that there was dehydration, together with removal of the most volatile products, including any unchanged aldol.

*Oxidation Experiments on Aldol Condensation Products.*—Qualitative tests showed that (i) ammoniacal silver nitrate was reduced very slowly at 50° and at a measurable rate at 100°, (ii) reduction of Fehling's solution occurred slowly at 100°, and (iii) bromine water and aqueous potassium permanganate were rapidly decolorised.

The following large-scale oxidations were attempted, and the reaction mixtures worked up chiefly with a view to isolating organic salts: (*a*) a 20% aqueous solution was treated with freshly precipitated silver oxide; (*b*) a concentrated aqueous solution was treated with bromine water, which led to the formation of strongly reducing material, acrid-smelling and lachrymatory, not sufficiently stable for isolation; (*c*) reaction with potassium permanganate, in aqueous or acetone solution, yielded no organic salts, though considerable quantities of potassium carbonate resulted from oxidative breakdown.

*Methylated Aldol Products.*—Trial experiments showed that methylation was possible with methyl alcohol containing 1% of hydrogen chloride, and that the methoxyl content of the product was increased from 12% to 16% by the use of carefully dried material and reagent. Similar products (OMe, 11%) were obtained by refluxing the aldol product with twice its weight of methyl iodide and an equivalent weight of silver oxide for several hours, or by treatment with excess of methyl sulphate and equivalent amounts of aqueous sodium hydroxide in methyl-alcoholic solution, though in the latter case it was difficult to avoid resinification. Further methylation of any of these products by similar treatment with methyl iodide or with methyl sulphate and alkali in the presence of alcohol, acetone or dioxan was not effected.

The following procedure was found to be the most satisfactory for large-scale preparations, in giving products with the highest and most consistent methoxyl content. Aldol material, previously heated for 8—10 hours at 45°/20 mm. with a current of dry air passing through, was dissolved in thirteen times its weight of dry methyl alcohol containing 0·7% of hydrogen chloride, and was kept for 12 hours at room temperature. After neutralisation with lead carbonate and filtration, the solution was evaporated at 45°/20 mm. and finally dried by heating for 1 hour at 50°/20 mm. The yield was 92% of the weight of dried starting material (approx. 100 g.) and the average methoxyl figure was 14%. The methyl-alcohol distillate obtained in this preparation invariably contained appreciable amounts of volatile material, possibly aldol dimethylacetal, which was neglected. It was frequently found that in spite of every attempt to adhere to a standard procedure, the products resulting were darker and more viscid and contained only 9% of methoxyl. These were thought to have been formed by initial polymeris-

ation of the aldol material in the presence of the traces of acid necessary for the methylation, and were not used for further investigation.

The methylated product was a pale yellow syrup of medium viscosity, soluble in organic solvents and very sparingly soluble in water. It was non-reducing towards silver nitrate and Fehling's solution, and only absorbed bromine from chloroform solution very slowly. Potassium permanganate in acetone solution was rapidly decolorised.

A fractional distillation of 80 g. was effected, the final distillation being carried out in a Widmer flask immersed in a carefully controlled bath, small fractions being collected over a narrow temperature range. Figures for typical lower fractions are given :

| Fract. | Press., mm. | Bath temp. | B. p. | Yield, g. | $n_D^{20.5°}$. | OMe, %. |
|---|---|---|---|---|---|---|
| 1 | 0·07 | 77—80° | 50—51° | 5·31 | 1·4464 | 19·2 |
| 3 | 0·06 | 90—110 | 50 | 0·92 | 1·4519 | 17·4 |
| 6 | 0·12 | 106 | 82 | 1·06 | 1·4622 | 12·1 |
| 7 | 0·12 | 109 | 84 | 3·04 | 1·4616 | 11·5 |

*Investigation of Methyl Aldol Products.*—Qualitative tests on unfractionated material suggested the presence of unsaturated linkages, and the following methods were adopted in order to establish the existence of ethenoid links and, if possible, to assess them.

(*a*) Bromine absorption in chloroform proceeded slowly, requiring several hours to go to completion, the reagent being added in small quantities with time for complete absorption between successive additions. The reaction mixture developed acidity, which was less marked on repetition in carbon tetrachloride solution, where the rate of absorption was also decreased and amounted to less than half of that expected on the assumed molecular weight.

(*b*) Hydrogenation with a platinum oxide catalyst was found to be most effective in glacial acetic acid solution, ethyl- and methyl-alcoholic solutions also being tried, and was complete in 50 minutes. For the lower fractions the absorption measured corresponded to approximately half that expected for one double bond. For the higher fractions absorption was proportionally greater, but was not found to increase by prolonged heat treatment prior to the hydrogenation.

(*c*) Treatment of fractionated methyl aldol with dilute aqueous or dry acetone solution of potassium permanganate showed an oxygen absorption roughly corresponding to the hydrogenation figures. Reaction was rapid at first and then slowed down considerably, not reaching an end-point for several hours.

*Acetylated Methyl Aldol Products.*—Preliminary experiments indicated the necessity for vigorous conditions for acetylation, modified procedures in which similar reaction mixtures were heated for 1—3 hours at 50—100° being unsatisfactory, since, although it seemed probable that some reaction had occurred, yet the products retained many of the characteristic properties of untreated methyl aldol material, and could not be satisfactorily separated, as was the case with those to be described.

A mixture of unfractionated methyl aldol material (50 g.) with acetic anhydride (100 g.) and anhydrous sodium acetate (15 g.) was heated cautiously to 130°; reaction then set in, causing vigorous ebullition. The reaction was allowed to proceed to completion, heating was recontinued for 10 minutes, and most of the excess of acetic anhydride was then rapidly distilled off. The hot mixture was poured slowly into a large volume of well-stirred ice-cold water (4 l.), whereby a red viscid syrup separated, which was extracted with chloroform after 1 hour. The extract was washed free from acid and, on removal of the solvent, gave a reddish-brown, semi-viscid syrup, the yield corresponding to 116% by weight of the starting material.

Fractionation of the acetates was carried out similarly to that of the methyl aldol products, though in this case the more volatile products were distilled at 20 mm. because of their relatively greater volatility In the first distillation there was evidence of a separation, which appeared to be complete after the third fractionation, as indicated by b. p., refractive index, and analysis. From a consideration of the data, some of which are recorded below, the estimated yields of the two compounds isolated approximated to 10% and 20%.

| Fract. | Press., mm. | Bath temp. | B. p. | Yield, g. | $n_D^{20.5°}$. | Fract. | Press., mm. | Bath temp. | B. p. | Yield, g. | $n_D^{20.5°}$. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 22 | 131° | 107° | 2·69 | 1·4260 | 7 | 20 | 139 | 108° | 3·23 | 1·4466 |
| 2 | 21 | 131 | 107 | 2·35 | 1·4279 | 8 | 0·14 | 106 | 83 | 5·32 | 1·4463 |
| 5 | 19 | 139 | 109 | 0·77 | — | 9 | 0·17 | 108 | 83·5 | 5·91 | 1·4457 |

These acetyl derivatives were colourless syrups, the lower fractions mobile with fragrant smell, higher fractions (not shown in the table) more viscid and not sweet-smelling. They were all insoluble in water and readily soluble in organic solvents, non-reducing towards Fehling's

solution or ammoniacal silver nitrate, and did not undergo hydrogenation. There was no reaction with bromine in chloroform or with potassium permanganate in acetone, except after long standing; reaction then slowly developed and thereafter proceeded at a measurable rate.

From three such complete fractionations it was possible to obtain, in equivalent yields, fractions thought to contain chemically pure individuals as shown by constancy of b. p. and refractive index. These were the acetylated methyl-laetolides I and II referred to in the discussion.

*Acetate* I, obtained from fraction (2) above by redistillation, was a very hygroscopic, pleasant-smelling, colourless, mobile liquid, b. p. 107°/21 mm., $n_D^{20.5°}$ 1·4270 [Found: C, 56·7; H, 8·2; OMe (max.), 16·3; Ac, 31·6 by alkaline estimation, 28·5 by acid hydrolysis; *M*, in benzene, 186. $C_9H_{16}O_4$ requires C, 57·5; H, 8·5; OMe, 16·5; Ac, 22·9%; *M*, 188].

*Acetate* II, obtained from fraction (8) above by redistillation, was a hygroscopic, slightly viscid liquid, less fragrant-smelling than acetate I, b. p. 83°/0·15 mm., $n_D^{20.5°}$ 1·4460 [Found: C, 57·5; H, 8·1; OMe (max.), 11·6; Ac, 35·8 by alkaline estimation; *M*, in benzene, 270. $C_{13}H_{22}O_6$ requires C, 56·9; H, 8·0; OMe, 11·3; Ac, 31·3%; *M*, 274].

*Comments on analytical figures.* (a) C and H figures were very consistent for samples of different batches and are in much better agreement with those required for higher homologues in each case, *i.e.*, acetate I as $C_{13}H_{22}O_6$ and acetate II as $C_{17}H_{28}O_8$. In spite of rigorous fractionation acetate I always gave a slight acid reaction, thought to be due to acetic acid, which might explain the low carbon figure. Acetate II gave no such acid reaction and for its high carbon value some other explanation is necessary, the analytical figures for various samples being equally consistent.

(b) Zeisel estimations were carried out with the utmost care by semi-micro-methods. It was necessary in all cases to start the reaction in the cold and to warm very gradually to avoid resinification as far as possible. In order to reach an end-point, it was necessary to continue the reaction for 3 hours, the formation of methyl iodide being very slow after the first hour. Typical figures for acetate II are: 9·6, 10·9, and 11·6% for 1, 2, and 3 hours respectively.

(c) Deacetylation proceeded very readily, but it was difficult to achieve a quantitative estimation owing to the possibility of further reaction with alkali or, in the case of acid hydrolysis, to avoid complications by simultaneous demethylation. For macro-acetyl determinations N/10-sodium hydroxide or -barium hydroxide was used, the reaction being allowed to proceed for 1 hour at 50°, in aqueous acetone solution and in an atmosphere of nitrogen. Consistent figures were obtainable in spite of the appearance of a yellow indicator-like side product, which somewhat obscured the end-point of the titration.

Comparative micro-acetyl estimations using acid or alkaline hydrolysis gave lower values in the former case.

(d) Molecular-weight determinations on the acetates were made by cryoscopic methods in benzene, glacial acetic acid, and camphor as solvents. In acetic acid precaution was taken to exclude atmospheric moisture, yet the values obtained were lower than those in benzene, *e.g.*, acetate I 174 and 186 respectively, and decreased with concentration, *e.g.*, 177 for 0·1847 g. and 169 for 0·2971 g. in 25 g. of solvent. In benzene solution results were more consistent, yet lower values were obtained after several hours than immediately after solution; *e.g.*, for acetate II, 220 ⟶ 270.

The author wishes to express her thanks to Professor T. S. Moore for his interest and encouragement in this work, and to the Distillers Company, who kindly furnished material for the investigation.

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## **108.** *Reduction Products of the Hydroxyanthraquinones. Part XV. Green Vat Dyes derived from Thiophen and* 3-*Substituted* 4-*Hydroxyanthranols.*

By (the late) ARTHUR GEORGE PERKIN and NORMAN HULTON HADDOCK.

The interaction of 4-hydroxy-3-methoxyanthranol, or 4 : 4′-dihydroxy-3 : 3′-dimethoxydianthrone, and tetrachloro- or tetrabromo-thiophen, or of 3 : 4-dihydroxyanthranol with methyl sulphate, anhydrous sodium carbonate, and commercial tri-

**chlorobenzene (containing chlorothiophens) gives a green vat *dye*, for which a constitution is suggested. A green *dye* of analogous constitution is obtained from 4-hydroxy-3-methylanthranol and commercial trichlorobenzene.**

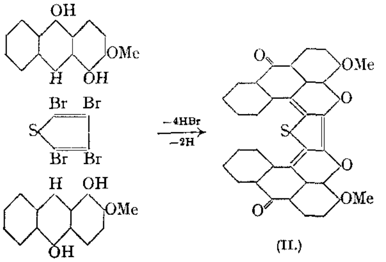
DURING experiments with the object of methylating 3 : 4-dihydroxyanthranol (I) by means of methyl sulphate and anhydrous alkali carbonate, commercial trichlorobenzene was used as a solvent. The result was unexpected, for, as heating proceeded, a dark green vat dye was progressively precipitated. It thus appeared likely that the methylated anthranol at first produced had reacted with some constituent of the crude trichlorobenzene, and such a view was confirmed by digesting 4-hydroxy-3-methoxyanthranol in this solvent, the same dye being obtained, but no reaction occurred with 3 : 4-dimethoxyanthranol. Fractions derived from this technical trichlorobenzene consisted mainly of 1 : 3 : 5-, 1 : 2 : 3-, 1 : 2 : 4-trichlorobenzenes, and 1:2:3:4-tetrachlorobenzene, and each reacted in this way with 4-hydroxy-3-methoxyanthranol, but the pure chloro-compounds specially prepared for this purpose gave negative results. The clue to the nature of the condensation was indicated by the presence of sulphur in the pure dye, which suggested the reactant to be a chlorothiophen, crude benzene having evidently been employed for the production of the technical trichloro-compound. The subsequent preparation from thiophen itself of tetrachlorothiophen, which with 4-hydroxy-3-methoxyanthranol in nitrobenzene solution readily yielded this green dye, undoubtedly proved it to be the reactant in question. The condensation of tetrachlorothiophen with 4-hydroxy-3-methoxyanthranol proceeded with evolution of hydrogen chloride, the dye produced being free from halogen, and indeed an identical compound was obtained when tetrabromothiophen was employed. Recrystallised from much nitrobenzene, this dye, here termed the "*methoxy-green*" *dye*, forms fine needles with a coppery lustre, insoluble in dilute alkali, and giving a blue vat with alkaline hyposulphite. The analytical results support the formula $C_{34}H_{18}O_6S$, and appear to suggest that the reaction occurs between two molecules of 4-hydroxy-3-methoxyanthranol and one molecule of the tetrahalogenothiophen, thus,

$$2C_{15}H_{12}O_3 + C_4Br_4S = C_{34}H_{20}O_6S + 4HBr$$

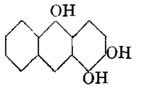
this passing by further oxidation into the colouring matter (II). Experiment has shown, however, that 4 : 4′-dihydroxy-3 : 3′-dimethoxydianthrone, which previous work has indicated is likely to be produced from the anthranol by air oxidation in the hot solvent during the digestion, reacts in these circumstances as well as, if not better than, the anthranol. Dye formation will thus occur directly :

$$C_{30}H_{22}O_6 + C_4Br_4S = C_{34}H_{18}O_6S + 4HBr.$$

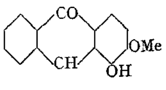
The condensation with the anthranol can be expressed as follows :




(II.)




(I.)




(III.)

and in a similar manner with the dianthrone the free radical (III) comes into play. Formula (II) is of interest, as it contains not only a thiophen residue, but also two pyran nuclei. Although the presence of the latter was indicated by the absence of hydroxyl groups in the dye, more certain evidence was given by the fact that, when the dye was

cautiously oxidised with chromic acid, alizarin 2-methyl ether was the main product. It is noteworthy that, although numerous preparations of the dye were made by one of us (A. G. P.), the analytical results for methoxyl were always low. It was thus evident that, under the experimental conditions employed, it was impossible to obtain a pure compound.

For the reaction with a tetrahalogenothiophen to occur, the presence in the anthranol of the 4-hydroxy-group is essential. The behaviour of 4-hydroxy- and 1 : 5-dihydroxy-anthranols with tetrachlorothiophen was studied, but dye formation did not occur in the latter case and only to a small extent in the former. This suggested that in the case of 4-hydroxy-3-methoxyanthranol the methoxy-group has a directing influence on the course of the reaction and does not merely enhance the chromophoric effect in the resulting dye. It was thus of interest to study the behaviour of the methyl group in this respect, and for this purpose 4-hydroxy-3-methylanthranol, readily prepared from *1-acetoxy-2-methyl-anthraquinone* by the method of Cross and Perkin (J., 1930, 292), was employed. From this, by digestion with technical trichlorobenzene, a dye, similar in character to the "methoxy-green" discussed above, was produced in almost theoretical yield; it is here distinguished as the "*methyl-green*" *dye*. The "methyl-green" dye, which was obtained as a coppery mass of fine flat needles, gave analyses corresponding with the formula $C_{34}H_{18}O_4S$, and can be represented in the same manner as (II) by replacing the two methoxy-groups by methyl groups. When it was oxidised gently with chromic acid, the main product was 1-hydroxy-2-methylanthraquinone, together with a little of a *substance*, greenish prisms, m. p. 300—303°, having apparently the formula $C_{34}H_{18}O_6S$, and traces of a *substance*, orange-yellow needles, m. p. 303—305°, which from the analytical data, m. p. and mixed m. p., and other properties, appeared to be either a modification of the former substance or to be closely related to it. In addition to alizarin 2-methyl ether, a trace of a similar yellow substance was isolated from the oxidation mixture of the "methoxy-green" dye.

Both dyes, the "methoxy-green" and the "methyl-green," dye cotton from a hyposulphite vat deep shades of considerable beauty and of a fairly permanent character, but these are less fast to light and hypochlorite solution than other well-known green vat dyes now on the market. Otherwise, owing to the simplicity of their methods of preparation, these new dyes would possess considerable technical importance. The process of manufacture of the "methoxy-green" dye is covered in B.P. 353,422, granted to Imperial Chemical Industries, Ltd., A. G. Perkin, A. Shepherdson, and N. H. Haddock.

## Experimental.

*4-Hydroxy-3-methoxyanthranol.*—A modification of the method of Cross and Perkin (J., 1930, 292) was employed. Acetyl alizarin 2-methyl ether (20 g.) in boiling glacial acetic acid (200 c.c.) was cooled to 90°, stannous chloride–hydrochloric acid (200 c.c. of a solution of 400 g. of stannous chloride in 1 l. of hydrochloric acid) added, and, after shaking, the mixture kept for 2 days. The deposit of 4-hydroxy-3-methoxyanthranol, m. p. 198—201°, was collected and washed (yield, 13·7 g.; 85%). The m. p. was raised to 203—204° by crystallisation from benzene. The acid stannous chloride filtrate on dilution gave mainly 1-hydroxy-2-methoxy-anthranol.

*Tetrachlorothiophen.*—Crude benzene (2 l.) was treated with bromine (120 g.) (cf. Meyer and Stadler, *Ber.*, 1885, **18**, 1489), and the nearly pure dibromothiophen (30 g.), b. p. 203—207°, isolated by the method of these authors. From this, by the action of excess of chlorine below 30° (Weitz, *Ber.*, 1884, **17**, 795), the tetrachloro-compound was obtained; after re-crystallisation it melted at 38° (Weitz gives 36°).

*Tetrabromothiophen.*—Tetrabromothiophen was prepared from thiophen by direct bromination and melted at 116° (Meyer and Kreis, *Ber.*, 1883, **16**, 2172, give m. p. 112°).

*The "Methoxy-green" Dye.*—(a) A mixture of 3 : 4-dihydroxyanthranol (20 g.), commercial trichlorobenzene (400 c.c.), anhydrous sodium carbonate (30 g.), and methyl sulphate (30 g.) was well stirred and heated at 190—200° for 3 hours. The green precipitate was collected and washed with water (yield, 7·5 g.). Longer digestion (4 hours) gave an increased yield (19·9 g.) of a less pure substance. On account of its sparing solubility in nitrobenzene, the product was suspended in a calico bag under reflux and extracted with the boiling solvent for 24 hours. The crystals were collected and washed with alcohol (yield, 10 g.).

(b) 4-Hydroxy-3-methoxyanthranol (1 g.) and tetrachlorothiophen (1 g.) were dissolved in hot naphthalene, the mixture boiled for 5 hours, and the *dye* isolated by means of hot benzene (yield, 0·7 g.) (Found: C, 73·0; H, 3·4; S, 5·5; OMe, 9·2. $C_{34}H_{18}O_6S$ requires C, 73·6; H, 3·3; S, 5·75; OMe, 11·1%). By a similar procedure with tetrabromothiophen (2 g.), an analogous result was obtained (Found: C, 73·4; H, 3·5; S, 6·3; OMe, 8·15%).

(c) 4 : 4′-Dihydroxy-3 : 3′-dimethoxydianthrone (0·2 g.), anhydrous sodium carbonate (0·3 g.) and commercial trichlorobenzene (3 c.c.) were stirred together and heated at 190—195° for 3 hours. The green precipitate (0·15 g.) was collected and washed with alcohol and finally with water. The product was identical in reactions with those obtained under (a) and (b).

*Oxidation of the "Methoxy-green" Dye.*—The "methoxy-green" dye (5 g.) was ground into a paste with glacial acetic acid, the suspension diluted to 75 c.c. and heated to 75°, and a solution of chromic acid (3·5 g.) in acetic acid (32 c.c.) and water (3 c.c.) added in portions (5 c.c.) during 45 minutes, the temperature being kept almost constant throughout and for a further 15 minutes. After 12 hours, the residue (A) (2·8 g.) was collected. The filtrate was diluted with water and gave a dull orange-brown powder (0·8 g.). The latter was extracted with boiling benzene and filtered (charcoal), benzene removed from the filtrate, the residue dissolved in alcohol, and the solution concentrated. The orange-red product was acetylated in presence of pyridine for 1 hour, and the liquid (charcoal) filtered and diluted with alcohol. Recrystallisation oi the product from alcohol–acetic acid gave acetyl alizarin 2-methyl ether in pale yellow needles, m. p. 203—205° (Found: C, 69·1; H, 4·0. Calc. for $C_{17}H_{12}O_5$: C, 69·5; H, 4·1%). This was converted by hydrolysis with hydrochloric acid into alizarin 2-methyl ether, orange-red needles, m. p. 228—230° (Found: C, 70·9; H, 4·0. Calc. for $C_{15}H_{10}O_4$: C, 71·2; H, 4·0%).

The residue (A) consisted mainly of uuattacked "methoxy-green" dye, but after digestion with much boiling glacial acetic acid the extract deposited a small amount of fine yellow crystals. These dissolved in boiling pyridine, and on addition of alcohol separated in a purer condition, but in too small amount for examination.

1-*Hydroxy*-2-*methylanthraquinone*.—This compound, obtained by Bentley, Gardner, and Weizmann (J., 1907, **91**, 1635) from *o*-cresol and phthalic anhydride, was prepared from 1-amino-2-methylanthraquinone (100 g.) in sulphuric acid (1000 g.) by gradual diazotisation with sodium nitrite (33 g.) at room temperature, and decomposition of the product by addition of water (5%) and heating at 90° for 5 hours. On dilution with much water, crude 1-hydroxy-2-methylanthraquinone, m. p. 178—180°, separated (yield, 94·5%). After purification *via* the acetyl compound, the m. p. was 184° (cf. Bentley, Gardner, and Weizmann, *loc. cit.*).

1-*Acetoxy*-2-*methylanthraquinone*, prepared in the usual manner, crystallised in pale yellow needles, m. p. 187—189° (Found: C, 72·6; H, 4·5. $C_{17}H_{12}O_4$ requires C, 72·8; H, 4·3%).

4-*Hydroxy*-3-*methylanthrone*.—To the above acetoxy-compound (10 g.) in glacial acetic acid (100 c.c.) at 90°, stannous chloride (30 g.) in hydrochloric acid (70 c.c.) was added. After 2 days, the product, almost colourless needles, m. p. 197°, was collected (yield, 92·6%).

*The "Methyl-green" Dye.*—A solution of 4-hydroxy-3-methylanthrone (10 g.) in commercial trichlorobenzene (100 c.c.) (containing 3·36% of sulphur, equivalent to 8·8% of thiophen), which at 170° gave evidence of dye formation, was boiled (195°) for 5 hours. The collected product was washed with alcohol (yield, 5·4 g.). When a larger volume of commercial trichlorobenzene (260 c.c.) was used with addition of potassium acetate (10 g.), the yield was increased (11·08 g.). The "*methyl-green*" *dye* was recrystallised from much nitrobenzene, in which it is more soluble than the "methoxy-green" dye (Found: C, 77·7; H, 3·6; S, 6·1. $C_{34}H_{18}O_4S$ requires C, 78·1; H, 3·5; S, 6·1%. $C_{34}H_{20}O_4S$ requires C, 77·9; H, 3·8; S, 6·1%).

*Oxidation of the "Methyl-green" Dye.*—The "methyl-green" dye (3 g.) was ground into a cream with glacial acetic acid (45 c.c.) and a solution of chromic acid (2·5 g.) in glacial acetic acid (30 c.c.) containing a little water was gradually added during 1 hour at 70°. After keeping overnight, the residue (A) (1·05 g.) was collected. The filtrate was diluted with water and gave a dull orange product (1·25 g.), which was extracted with benzene (charcoal) and filtered, and benzene removed from the filtrate. The resulting residue was boiled with much alcohol; a little red powder (B) (0·05 g. approx.) was then deposited. The alcoholic filtrate on concentration gave crystals, converted by acetylation and recrystallisation from alcohol–acetic acid into 1-acetoxy-2-methylanthraquinone, pale yellow needles, m. p. 187—189°, hydrolysed to 1-hydroxy-2-methylanthraquinone, m. p. 184—185° (Found: C, 75·6; H, 4·3. Calc. for $C_{15}H_{10}O_3$: C, 75·6; H, 4·2%).

Residue (B), after two crystallisations from benzene, consisted of small greenish prisms,

m. p. 300—303° (Found: C, 73·5; H, 3·45; S, 5·4. $C_{34}H_{18}O_6S$ requires C, 73·6; H, 3·3; S, 5·7%), insoluble in alkalis, but soluble in sulphuric acid with a dull red tint, becoming green at the edges on keeping. The residue (A) was extracted with a large amount of boiling benzene and left much "methyl-green" dye undissolved. The extract (charcoal) on concentration gave orange-yellow needles, which after recrystallisation melted at 303—305° (C) (Found: C, 73·5; H, 3·4; S, 5·4. $C_{34}H_{18}O_6S$ requires C, 73·6; H, 3·3; S, 5·7%), and dissolved in sulphuric acid with a dull red tint, becoming green at the edges; it gave with alkaline hyposulphite a yellow liquid and had *similar* properties to (B). The mixed m. p. of (B) and (C) was 300°, and possibly (B) is slightly impure (C), or a modification of it.

The authors acknowledge gifts of material from Imperial Chemical Industries, Ltd., and the help given by Mr. W. W. Tatum (of Imperial Chemical Industries, Ltd., Dyestuffs Group), who prepared the "methyl-green" dye, and by Mr. C. Hollins (of Imperial Chemical Industries, Ltd.), who suggested that the reactant in technical trichlorobenzene was a chlorinated thiophen. One of the authors (N. H. H.) desires to thank Imperial Chemical Industries, Ltd., for permission to publish this paper.

THE UNIVERSITY, LEEDS.
RESEARCH LABORATORIES, BLACKLEY. [*Received, February 15th*, 1938.]

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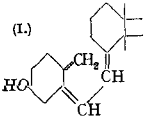
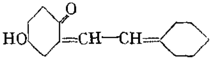
# NOTES

## *Preliminary Note on the Synthesis of Compounds Related to the Antirachitic Vitamins. The Condensation of* cyclo*Hexylideneacetaldehyde with 4-Hydroxy*cyclo*hexanone.* By JOHN B. ALDERSLEY and G. NORMAN BURKHARDT.

As the first stage in an investigation directed to the synthesis of compounds of the general formula (I), containing the conjugated system of calciferol, the ketone (II) has been obtained by

(I.)





(II.)

condensation of *cyclo*hexylideneacetaldehyde [b. p. 80—85°/16 mm.; main absorption band, in alcohol, $\lambda = 2390$ A., $\varepsilon = 9,100$; *semicarbazone*, m. p. 205° (Found: C, 59·4; H, 7·9; N, 22·7. $C_9H_{15}ON_3$ requires C, 59·6; H, 8·3; N, 23·2%); $\lambda_{max.} = 2720$ A., $\varepsilon_{max.} = 28,000$] with 4-acetoxy*cyclo*hexanone [b. p. 121—124°/11 mm.; *semicarbazone*, m. p. 182—183° (Found: N, 19·8. $C_9H_{15}O_3N_3$ requires N, 19·7%)] in presence of excess of aqueous sodium hydroxide. The product was characterised by its absorption spectrum ($\lambda = 3060$ A., $\varepsilon = 10,530$, in alcohol), its *phenylurethane*, m. p. 180° (Found: C, 74·6; H, 7·5; N, 4·2. $C_{21}H_{25}O_3N$ requires C, 74·5; H, 7·4; N, 4·1%), and its 2 : 4-*dinitrophenylhydrazone*, m. p. 170—171° (Found: N, 13·9. $C_{20}H_{24}O_5N_4$ requires N, 14·0%). Preliminary experiments on the replacement of the carbonyl oxygen by an exocyclic methylene group have given a product having an absorption maximum at 2690 A., which compares favourably with that exhibited by calciferol (2650 A.).

*cyclo*Hexylideneacetaldehyde was obtained together with its isomer, *cyclo*hexenylacetaldehyde [b. p. 58—62°/16 mm.; *semicarbazone*, m. p. 186° (Found: C, 59·8; H, 8·1. $C_9H_{15}ON_3$ requires C, 59·6; H, 8·3%)], by the ozonolysis of 1-allyl*cyclo*hexanol (Mazurewitsch, *J. Russ. Phys. Chem. Soc.*, 1911, **43**, 973), separation of the products being effected by fractional distillation.

4-Acetoxy*cyclo*hexanone was prepared by chromic anhydride oxidation of quinitol monoacetate (4-*acetoxycyclohexanol*), which in its turn was obtained in good yield by the partial hydrolysis of *trans*-quinitol diacetate.—THE UNIVERSITY, MANCHESTER. [*Received, February 10th*, 1938.]

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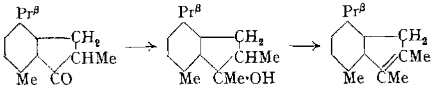
*The Preparation of* 1 : 2 : 7-*Trimethyl*-4-iso*propylindene and* 1 : 2 : 7-*Trimethyl*-4-iso*propylhydrindene.* By C. L. CARTER and S. N. SLATER.

THESE two compounds were prepared during an attempt to synthesise an azulene which was undertaken before the work of Pfau and Plattner appeared (*Helv. Chim. Acta*, **1936**, **19**, 858; **1937**, **20**, 224). 2 : 7-Dimethyl-4-*iso*propyl-1-hydrindone (Cook, Hewett, Mayneord, and Roe, J., **1934**, 1727) on treatment with methylmagnesium iodide yielded 1 : 2 : 7-*trimethyl*-4-iso*propylindene*, the tertiary alcohol first formed losing the elements of water:



Catalytic hydrogenation yielded 1 : 2 : 7-*trimethyl*-4-iso*propylhydrindene.* Attempts at dehydrogenation were unsuccessful.

The Grignard reagent prepared from methyl iodide (14 g.) and magnesium (2·4 g.) in ether (30 c.c.) was cooled in ice, and 2 : 7-dimethyl-4-*iso*propyl-1-hydrindone (10 g.) in ether (20 c.c.) added during 2 hours. After 2 hours' boiling, the product was decomposed with ice and concentrated hydrochloric acid and extracted with ether. The extract was freed from iodine by sodium bisulphite, most of the solvent removed, and the yellow oil steam-distilled. The distillate, dried in ether and distilled in a vacuum, had b. p. 154—157°/17 mm., $d_{25°}^{25°}$ 0·9574, $n_D^{25°}$ 1·5428 (Found: C, 90·6; H, 10·4. $C_{15}H_{20}$ requires C, 90·0; H, 10·0%).

1 : 2 : 7-*Trimethyl*-4-iso*propylindene* (5 g.) in alcohol was hydrogenated in the presence of freshly prepared palladised norit (0·5 g.). After 6 hours an absorption of 585 c.c. (corresponding with one double bond) took place. The product was removed and distilled in a vacuum, yielding 1 : 2 : 7-*trimethyl*-4-iso*propylhydrindene* as a clear, mobile, slightly yellow oil, b. p. (redistilled) 154—155°/29 mm., $d_{25}^{25°}$ 0·9250, $n_D^{25°}$ 1·5112 (Found: C, 88·85; H, 10·8. $C_{15}H_{22}$ requires C, 89·1; H, 10·9%).—UNIVERSITY OF OTAGO, NEW ZEALAND. [*Received, March 25th*, 1938.]

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*Thixotropic Behaviour of Silica Gels.* By HERBERT FREUNDLICH and DAVID W. GILLINGS.

IT has generally been considered that silica gels do not show any thixotropy (see, for instance, H. Freundlich "Thixotropy," Hermann, Paris, note 13 in bibliography). In agreement with this consideration, no liquefaction of silica gels by ultrasonic waves has previously been noted (Freundlich, Rogowski, and Söllner, *Kolloid Beih.*, **1933**, **37**, 215).

In the course of experiments on the reduction of viscosity of colloidal solutions by ultrasonics, we have found that these observations apply only to the acid gels, as they are formed when solutions of sodium silicate are mixed with an excess of hydrochloric acid. By dialysis of these sols, we obtained a product, slowly coagulating to a gel, which could be liquefied by shaking, or by ultrasonics, and returned to the gel state after the disturbance ceased.

As far as our experiments go, all these thixotropic gels were weakly alkaline, at the $p_H$ range 8·5—9·5. This is the range at which Freundlich and Cohn (*Kolloid-Z.*, **1926**, **39**, 28) showed that silica sols could be coagulated by electrolytes.—THE SIR WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES OF CHEMISTRY, UNIVERSITY COLLEGE, LONDON, W.C.1. [*Received, February 23rd*, 1938.]

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*The Reaction between Disodium Phthalocyanine and Methyl Alcohol.* By CHARLES E. DENT.

COLD methyl alcohol rapidly and completely eliminates the sodium from disodium phthalocyanine (Barrett, Dent, and Linstead, J., **1936**, 1719). The change within a few seconds from a thin suspension of the crystalline disodium phthalocyanine (1 part) in methyl alcohol (4 parts) to a thick paste of finely divided, amorphous, metal-free phthalocyanine is so marked that it can be used as a test for either compound. The final mixture is strongly alkaline. The reaction can be followed under a microscope with minute quantities of reagents, the dull green smear first produced rapidly changing to the bright blue colour of the dispersed metal-free pigment.

The reaction appears to be specific for methyl alcohol. Dilution with water or ethyl alcohol to 50% slows the reaction slightly. Many reagents, *e.g.*, wet ethyl alcohol, dilute acids, are known to cause sodium elimination (Barrett, Dent, and Linstead, *loc. cit.*), but in no case do they react with sufficient vigour to produce the above remarkable change in physical form.

A wide range of hydroxylic and other compounds has been brought into reaction with disodium phthalocyanine under various conditions and as mixtures. Only ethyl, butyl, and *n*-propyl alcohols gave, in decreasing order, any similar reactivity and then only on prolonged standing. Disodium phthalocyanine thus appears to be a very valuable " spot " reagent for methyl alcohol.

The author thanks Imperial Chemical Industries, Limited, and the Directors of the Dyestuffs Group for permission to publish this note.—[*Received, February* 14th, 1938.]

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*The Transition Temperatures of Lithium Chloride Hydrates.* By MALCOLM P. APPLEBEY and RALPH P. COOK.

RECENT determinations of the transition temperatures $LiCl \rightleftharpoons LiCl,H_2O$ and $LiCl,H_2O \rightleftharpoons LiCl,2H_2O$ show greater discrepancies than would be expected from the estimated accuracy of individual determinations. For the upper transition temperature, Applebey, Crawford, and Gordon (J., 1934, 1665) obtained a value of 93·5° ± 0·5° from measurements of solubility, density, and vapour pressure of saturated solutions, and from cooling curves, whereas Friend, Hale, and Ryder (J., 1937, 970) from solubility measurements give a transition temperature of 96°. The lower transition temperature determined by Applebey, Crawford, and Gordon is 19·1° ± 0·25° from solubility and density of saturated solutions and cooling curves, also in poor agreement with Friend and Colley's value (J., 1931, 3148) of 18° obtained by solubility measurements, and with the determination by Benrath (*Z. anorg. Chem.*, 1932, **205**, 417), who found the temperature of continued coexistence of the two solids with the saturated solution to be 20°. In view of these discrepancies, we have made some measurements by the dilatometric method.

The lithium chloride used contained a small amount of insoluble matter and traces of sulphate and of calcium salts. It was recrystallised from water and a product was obtained which was free from sulphate and contained only 0·02% of calcium. The monohydrate and dihydrate were prepared by crystallisation at appropriate temperatures, and the anhydrous salt by drying the monohydrate in an air-oven at 120—150°.

A mixture of approximately equal amounts of the two forms was confined in the bulb of the dilatometer by toluene at the lower temperatures, and by *m*-xylene at the higher temperatures. These liquids were purified by agitation with mercury to remove traces of sulphur, followed by distillation. The dilatometers were immersed in electrically regulated thermostats, the constancy of which at both temperatures was better than ± 0·01°; transformer oil was used for the bath liquid at the upper temperature. Temperatures were read by a Beckmann thermometer calibrated against a thermometer standardised by the N.P.L., and the rate of change of volume at a series of constant temperatures was observed. Measurements at temperatures comparatively remote from the transition point were taken over periods of an hour or more; close to the transition point the measurements extended over period varying from 4 to 24 hours. The readings obtained were as follows (A and B refer to two dilatometers charged with salt from separate preparations):

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Temp. ........... | 19·23° | 19·18° | 19·13° | 19·10° | 19·09° | 19·08° | 19·05° | 19·03° | 18·98° |
| Rate, cm./hr. { A ... | +17·4 | +11·7 | +5·5 | — | — | 0·00 | — | −1·0 | −7·8 |
| Rate, cm./hr. { B ... | — | — | — | +2·0 | +0·45 | +0·27 | −1·7 | — | — |
| Temp. ........... | 93·73° | 93·63° | 93·53° | 93·48° | 93·43° | 93·42° | 92·93° | 92·44° | |
| Rate, cm./hr. ... | +4·7 | +1·4 | +0·12 | −0·12 | −0·85 | −1·4 | −4·7 | −7·7 | |

From these measurements we conclude that the transition temperatures for the sample of salt used are 93·51° ± 0·03° for $LiCl \rightleftharpoons LiCl,H_2O$ and 19·07° ± 0·02° for $LiCl,H_2O \rightleftharpoons LiCl,2H_2O$. A correction may be applied for the small quantity of calcium present as impurity. Assuming that this is present as completely dissociated calcium chloride, and taking the heats of reaction as

$LiCl + H_2O \longrightarrow LiCl,H_2O: \Delta H = -4950$ (Applebey, Crawford, and Gordon, *loc. cit.*)
$LiCl,H_2O + H_2O \longrightarrow LiCl,2H_2O: \Delta H = -3162$ (Bogorodski, *J. Russ. Phys. Chem. Soc.*, 1893, **25**, 320)

we find a correction of + 0·04° in each case. Our final conclusion, therefore, is that the most probable values of the transition temperatures are 93·55° and 19·1° with an uncertainty of not more than ± 0·05° in each case.—BILLINGHAM. [*Received, February* 21st, 1938.]

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# ANNUAL GENERAL MEETING

THE Ninety-Seventh Annual General Meeting was held in the University of Manchester on Thursday, March 31st, 1938, at 4 p.m., the PRESIDENT, Professor F. G. DONNAN, C.B.E., D.Sc., F.R.S., occupying the Chair. The business portion of the meeting took place in the Staff House.

The notice convening the meeting was read.

The Report of Council for 1937 (see pp. 549—574) was presented, and the Treasurer, who was called upon by the President, dealt with the Accounts in detail. Taking first the General Purposes Account he remarked that the deficit was £757 as against £303 in 1936, and that the total income showed a decrease of £122 below that of the previous year, due to a reduction of £87 in the amount received as Life Composition Fees and to the Annual Subscriptions realising £34 less. On the expenditure side of the Accounts, there was an increase of £144 in the cost of administration and of meetings and of £121 in the contribution to the Publications Fund.

Dealing with the Publications Fund Account, the Treasurer stated that the total income exceeded that for 1936 by £852; of this, the sales of publications accounted for £410, increased revenue from advertisements for £59, and increased donations for £384. Passing to the expenditure side of the account, he referred to the increase of £371 in the cost of the *Journal* owing to an increase of 154 pages and to a 5 per cent. rise in printing charges and to the extra cost of *Abstracts* amounting to £693, which was due to dividing the Abstracts into three sections and providing two extra covers and also to an increase of 98 pages.

He referred to the considerable progress that had been achieved by the Chemical Council towards a satisfactory solution of the problems affecting the interests and activities of the three Constituent Bodies, stating that he was authorised to mention that a scheme for closer co-operation between the three Chartered Bodies had been drawn up by the Chemical Council, as a basis for discussion by the Councils of the three Bodies, who had the matter under consideration. The main object of the scheme was to render combined membership of the three bodies possible at a lower subscription than at present, and to allow to each member the option of a choice of the publications of the three bodies. It was hoped and expected that the scheme, if adopted, would in time attract sufficient new members to alleviate the financial difficulties of the publishing Societies due to the increasing cost of their publications. The funds placed at the disposal of the Chemical Council by Industry could be utilised to secure the financial stability of the new scheme in the early years.

In conclusion, he stated that though the present financial position was not too happy, there were reasonable indications that thanks to the prolonged and careful survey of the position of chemical publications made by the Chemical Council a permanent satisfactory financial basis of this side of the Society's activities would soon be established.

The Senior Secretary, in introducing the general sections of the Report of Council, dealt briefly with some of the activities of the Society during 1937. He stated that steps had now been taken to improve the *Annual Reports* and to render them more easily readable by the non-specialist; he referred to the changes that had been made in the form of the Proceedings, which now include a summary of the proceedings of Council, thus keeping Fellows more fully informed of the Council's deliberations. He also stated that the Council were now exploring other possible ways of providing further accommodation for library and administration purposes before deciding to give up the meeting room for these purposes. In conclusion he expressed the Council's appreciation of the services rendered by the permanent Officers of the Society and their respective staffs.

The adoption of the Report of Council for 1937, including Statements of Accounts and Balance Sheets, was proposed by Professor I. M. Heilbron, seconded by Dr. G. N. Burkhardt, and carried unanimously.

A vote of thanks to the Treasurer, Honorary Secretaries, Council, and Committees for their services during the year, proposed by Professor J. Kenner and seconded by Professor F. Challenger, was carried unanimously, Sir Gilbert Morgan making acknowledgment.

A vote of thanks to the Honorary Auditors (Dr. H. E. Cox, Dr. H. D. K. Drew, and Dr. G. Senter) for auditing the Accounts for 1937 was proposed by the Treasurer, seconded by Professor T. S. Moore, and carried. On the motion of the Treasurer they were re-elected for the ensuing year. Messrs. W. B. Keen & Co. were elected to audit the Accounts for the current financial year on the motion of Professor C. S. Gibson, seconded by Professor F. M. Rowe.

The report of the Scrutators on the ballot for the election of Ordinary Members of Council (Country Members) was presented and the President declared that new Members of Council had been elected as follows:

*Vice-Presidents who have filled the office of President:* Professor P. F. Frankland, Professor G. G. Henderson, Professor J. F. Thorpe.

*Ordinary Members of Council (Town Members):* Dr. A. G. Francis, Dr. R. J. W. Le Fèvre.

*Ordinary Members of Council (Country Members):* Dr. H. McCombie, Dr. E. B. R. Prideaux, Professor F. M. Rowe, Professor F. J. Wilson.

A vote of thanks to the Scrutators was proposed by Dr. T. A. Henry, seconded by Dr. H. Burton, and carried.

The proposed new Bye-Laws * which had been circulated to Fellows were then formally submitted to the meeting for approval. The senior Honorary Secretary dealt with the proposed changes and called attention to a further modification of Bye-Law 47 recommended by the Solicitors. He also stated that expressions of opinion received from Fellows regarding the proposed Bye-Laws had been received as follows:

| | | For. | Against. |
|---|---|---|---|
| I. | Proposals affecting the constitution of the Council ...... | 443 | 11 |
| II. | Proposals affecting the method of electing Fellows ...... | 439 | 17 |

A motion for the adoption of the new Bye-Laws as amended, proposed by Professor J. L. Simonsen and seconded by Dr. R. Fraser Thomson, was carried unanimously.

The President, Professor F. G. Donnan, then delivered his Presidential Address, entitled "Chemistry: Retrospect and Prospect," in the Chemistry Lecture Theatre of the University. At the conclusion of his Address, a vote of thanks to the President for his services in the Chair and for his Address was proposed by Professor N. V. Sidgwick, seconded by Professor M. W. Travers, and carried with acclamation.

A vote of thanks to the Council of the University of Manchester for hospitality was proposed by Dr. R. E. Slade, seconded by Professor G. Barger and carried, acknowledgment being made by Professor I. M. Heilbron. A vote of thanks to the Local Committee responsible for the arrangements of the Anniversary Meetings was proposed by Professor J. W. Cook, seconded by Dr. C. W. Davies, and carried, acknowledgment being made by Dr. D. W. Hill.

## REPORT OF COUNCIL, 1937.

During the year agreement was reached on two matters which had previously been examined in collaboration with other Societies. An Agreement was entered into with the Physiological Society, the Biochemical Society, and the Society of Chemical Industry for the re-constitution of the Bureau of Chemical Abstracts under the new title of the Bureau of Chemical and Physiological Abstracts, and for the enlargement of Abstracts A III, to include Physiology as well as Biochemistry. A joint committee on which the Society collaborated with the Physical Society and the Faraday Society issued a report on physico-

* The new Bye-Laws, as adopted, will be printed and issued to Fellows in due course.

chemical symbols which has been adopted by the three Societies as a statement of recommended usage in their publications.

Two special Committees have reported during the year on possible ways of improving and extending the services of the Society. On the recommendation of these Committees, and with the financial support of the Chemical Council, arrangements have been made whereby every paper appearing in the *Journal* is now accompanied by a short summary of its contents, and preliminary steps have been taken towards finding a solution of the serious problem of Library accommodation. Other proposals submitted by the Committees raised the question of the relations between the Society, the Institute of Chemistry, and the Society of Chemical Industry, and further consideration of these proposals has been deferred until the Chemical Council has explored the possibility of introducing a general scheme for the co-ordination of some of the services of the three constituent Bodies. In the meantime the amount of matter published in the *Journal*, and especially in Abstracts " A " continues to grow. Meetings in London have been better attended, and the increase in the number of meetings held in other centres is a satisfactory feature.

Consideration has recently been given to the desirability of altering the constitution of Council by introducing a scheme for territorial representation, and of changing the system for the election of Fellows to the Society. Details of the proposed changes will be communicated to Fellows, and recommendations regarding the corresponding revision of the Bye-Laws will be submitted.

## I. FELLOWSHIP.

### (1) *Fellowship Statistics.*

The number of Fellows on 31st December, 1936, was 3746. During 1937, 221 Fellows were elected and 14 reinstated, the corresponding figures in 1936 being 205 and 22, respectively. The Society has lost 48 by death, 109 by resignation, and 49 by removal for non-payment of annual subscriptions, the total loss of 206 being the same as in the previous year.

The number of Fellows on December 31st, 1937, was 3775, showing a net increase of 29.

The names of those Fellows who during the year have completed 60 and 50 years of Fellowship have been announced at the Ordinary Scientific Meetings and have been published in the Proceedings.

### (2) *Honours.*

The congratulations of the Society were conveyed to the following Fellows whose names were included in the lists of Coronation and New Year Honours :

| | |
|---|---|
| Dr. J. W. Mellor | C.B.E. |
| Sir David Milne-Watson | Baronet |
| Mr. Andrew More | I.S.O. |
| Mr. John W. Napier | M.B.E. |
| Col. Clive Newcomb | C.I.E. |
| Dr. Robert H. Pickard | Kt. |
| Mr. T. L. D. Porter | M.B.E. |
| Mr. P. F. Rowsell | C.B.E. |
| Mr. Duncan R. Wilson | Kt. |
| Mr. William F. Wyley | Kt. |

The Council also conveyed its congratulations to Professor W. N. Haworth on being awarded jointly with Professor P. Karrer the Nobel Prize for Chemistry, to Sir Robert Pickard on his election as Vice-Chancellor of the University of London, and to Professor N. V. Sidgwick on his being awarded a Royal Medal by the Royal Society.

### (3) *Deaths.*

During the year the Council has had to mourn the loss of its distinguished *Past-President*, Professor H. E. Armstrong, who, elected as a Fellow in 1870, was the doyen of the Society.

A resolution passed by the Council in October expressing its profound sorrow was communicated to the Ordinary Scientific Meeting on 21st October and conveyed by the President to the relatives. An obituary notice will be published in the *Journal.*

The Council has also to mourn the loss of four of its distinguished *Honorary Fellows* during the year:

Professor Edward Curtis Franklin, elected in 1903; died on 13th February.
Professor Amé Pictet, elected in 1923; died on 11th March.
The Right Hon. Lord Rutherford of Nelson, elected in 1929; died on 19th October.
Professor Jean Baptiste Senderens, elected in 1920; died on 26th September.

Resolutions passed by the Council were communicated to Fellows at the Ordinary Scientific Meetings and the condolences of the Council have been conveyed to the relatives. Memorial lectures or obituary notices have been arranged.

## II. PUBLICATIONS.

### (1) *Journal.*

(a) *Report of the Publication Committee.*

The *Journal* for 1937 contains 2016 pages (1862), of which 1865 pages (1765) are occupied by 425 memoirs (414) and 18 notes (28). [The numbers in parentheses above are the corresponding figures for 1936.] There are also 5 lectures (50½ pages), the Presidential Address (6 pages), the Report of the Annual General Meeting (20 pages), reports on atomic weights and isotopes (19½ pages), and Obituary Notices (55 pages). The 425 memoirs comprise 119 dealing with General, Physical and Inorganic Chemistry and 306 dealing with Organic Chemistry.

During 1937, 433 papers were received; 7 of these were declined.

The average interval between receipt and publication of the papers in 1937 was 9·2 weeks (10·0, 9·8, 9·5, and 9·4 weeks for 1936, 1935, 1934, and 1933 respectively).

For convenience in noting references the Committee has arranged that, from January 1938, the year number shall be printed on each page of the *Journal.*

(b) *Summaries of Papers in the Journal.*

The authors of all papers submitted after June 1st have been required to furnish short summaries of their papers, setting forth briefly and in simple language the objects of the investigations, the results obtained, and their bearing on chemical knowledge in general. The response by authors has been excellent, and it is believed that the summaries will be of material help to all readers of the *Journal.* In particular, it is hoped that they may enable chemists who have not the leisure or the equipment to read specialised papers in detail, still to keep abreast of the general progress of the subject.

### (2) *Abstracts.*

The Report of the Bureau of Chemical Abstracts for 1937 is reproduced in full as Appendix B of this Report.

As already announced to Fellows, an Agreement has been entered into between the Physiological Society, the Biochemical Society, the Society of Chemical Industry, and this Society, under the terms of which *Physiological Abstracts*, which has hitherto been issued as a separate publication by the Physiological Society, will henceforth be incorporated with British Chemical Abstracts " A," issued by the Bureau of Chemical Abstracts.

In accordance with this, the Bureau of Chemical Abstracts has been re-constituted, and will be known as *The Bureau of Chemical and Physiological Abstracts*; it has been enlarged by the addition of two representatives appointed by the Physiological Society.

Section A III, which has hitherto consisted of Abstracts in Biochemistry, will also include abstracts in Physiology, and will be entitled " A III. Physiology and Biochemistry." This section will be available to members of the Physiological Society and of the

Biochemical Society at special subscription rates, and to Fellows of the Chemical Society free of charge.

A combined general index covering Pure and Applied Chemistry will be issued as heretofore, but will also include Physiology.

As from the beginning of 1938, the three sections of British Chemical and Physiological Abstracts " A " will be as follows:

Section A I: General, Physical and Inorganic Chemistry,
Section A II: Organic Chemistry,
Section A III: Physiology and Biochemistry.

Facilities have been given for Fellows to obtain additional copies at special rates, and also to procure Abstracts printed on one side of the paper *instead of* or *in addition to* those printed on both sides of the paper.

Every Fellow receiving *British Chemical and Physiological Abstracts " A "* is now asked to give an undertaking that all copies of the Abstracts supplied to him are for his own use, and will not be sold by him within 12 months of the date of issue. Such copies are marked " Member's Copy."

### (3) *Annual Reports.*

Volume XXXIII of the *Annual Reports* for 1936 was published in April. It contained 469 pages compared with 485 pages in the previous volume.

The Publication Committee has had under review the arrangements for producing the Annual Reports, but had not completed its deliberations by the end of the year. It is expected that the changes in view will come into operation in the production of the Reports for 1938. The intention of the Committee is to introduce features which will make the Reports more interesting to the non-specialist without diminishing their value for those who require detailed summaries.

### (4) *Symbols and Conventions.*

The Report of the Joint Committee of the Chemical Society, the Faraday Society, and the Physical Society on " Symbols for thermodynamical and physico-chemical quantities and conventions relating to their use " was issued in June, and has been adopted as a statement of recommended practice in the *Journal of the Chemical Society* and in *British Chemical and Physiological Abstracts*, as well as in the *Proceedings of the Physical Society* and the *Transactions of the Faraday Society.*

In submitting its report, the Joint Committee draws attention to the fact that committees which have dealt with this subject in the past have nearly always been representative of *either* physicists *or* chemists, and not, as in the present instance, of both. A considerable measure of agreement between British chemists and physicists has now been attained in regard to the use of different alphabets and founts for the various classes of symbols and abbreviations, as well as to the actual symbols for particular quantities. Adoption of the report by the three co-operating Societies represents an important step towards uniformity of usage, and it is hoped that it may lead to a wider measure of agreement with workers in other branches of science and technology.

Copies of the report were issued to Fellows in pamphlet form with the *Journal* for August, and the lists of the recommended symbols is reprinted in the Index number of the *Journal.* Extra copies of the Report may be purchased by Fellows at special rates.

### (5) *Prices of Publications.*

The prices to be charged for the publications of the Society to Fellows and to members of certain cognate Societies and to the public have been correlated and revised.

## III. MEETINGS.

### (1) *Scientific Meetings.*

The Society has held 18 meetings in London during 1937. These included 5 Lectures, and 12 Ordinary Scientific Meetings. Of the latter, 4 took the form of organised Discussions, and at the other 8 meetings 25 papers were read and discussed. A visit to the Rothamsted Experimental Station at Harpenden was also arranged.

As an experiment, the Council decided that the Discussion held on 4th February should commence at 5 p.m. Arrangements were made for those present to dine together. The good attendance showed that this arrangement met with approval, and it was decided that two of the Discussions arranged for the session 1937–1938 should be held at this hour.

Meetings held outside London included 27 Lectures and 3 meetings for the reading of papers. The series of Bedson Lectures given at Newcastle-on-Tyne were also open to Fellows.

A complete list of Lectures and Discussions is given in Appendix D.

### (2) *Anniversary Meetings.*

A report of the Anniversary Meetings held in London from 17th to 19th March appeared in the *Journal* and *Proceedings* for that month. The cordial thanks of the Council were conveyed to Professor V. M. Goldschmidt for delivering the Seventh Hugo Müller Lecture; to the Court and Senate of the University of London for granting permission for the Society to hold the Social Evening in the University new buildings; and to the Royal Institution for the use of the Lecture Theatre. Thanks were also conveyed to the Anglo-Iranian Oil Co., the Gas Light & Coke Co., Messrs. J. Lyons & Co., the Mond Nickel Co., the Imperial College and University College, London, for giving facilities for visits to their establishments and for hospitality provided.

The Council has accepted an invitation from Fellows in Manchester to hold the Anniversary Meeting of the Society in that city in 1938.

## IV. LIBRARY.

The Report of the Joint Library Committee for 1937 is printed as Appendix C of this Report.

### *Library Accommodation.*

The question of Library accommodation referred to in last year's report has been investigated, and a report submitted to the Council of the Chemical Society and to the Chemical Council.

The Rooms of the Chemical Society are those allotted in 1873, when the membership was 682 and the Library contained about 3000 volumes. The Library now contains over 41,000 bound volumes, is growing at the rate of over 1000 bound volumes per annum, and is used by the members of eight Societies.

Space has been found for books in devious ways, but a position has now been reached when it is impossible to accommodate any more, and many volumes are unsuitably housed.

About one-half of the books are in steel rolling stacks in two basement rooms below street level with windows on the area facing Piccadilly. Should a fire occur or a water-main burst in the neighbourhood, there would be serious risk of irreparable damage through flooding. The Joint Library Committee concluded that the only satisfactory solution was to provide accommodation elsewhere for the whole Library. The Council of the Chemical Society has agreed, in principle, to the provision of other accommodation, and the Chemical Council has authorised the expenditure of a sum not exceeding £50 for the preparation of draft plans.

The scheme which the Joint Library Committee has in view would involve the raising of a very large sum of money, and in the meantime the possibility of using the Meeting Room for storage purposes has been under consideration, and plans have been prepared and submitted to His Majesty's Office of Works. This expedient, if sanctioned, would give

only temporary alleviation, and would necessitate the meetings of the Society being held elsewhere.

## V. OTHER ACTIVITIES.

### (1) *Grants for Research.*

In accordance with the decision of Council, the Research Fund Committee met this year in November instead of in December as in previous years. 71 applications for grants for research amounting to £770 were received and grants amounting to £645 were made. The list of grants made appeared in the *Proceedings* for November.

### (2) *General Services.*

The Special Committee to consider ways and means of increasing the membership of the Society, referred to in the last Report, presented a report to Council in February. Arising out of its recommendations, the Council decided to include summaries to papers in the *Journal*, and this came into practice in July. The Council also appointed a second Special Committee to consider proposals for improving the various services maintained by the Society, the cost of putting such proposals into effect and the arrangement of them in order of priority: this Committee held three meetings, and reported to Council in October. Some of its proposals, such as the drawing up of plans for re-housing the library, were duly adopted. In the forefront of its report, however, the Committee expressed the view that the realisation of its detailed recommendations for the improvement of individual services would be facilitated if it were possible to establish some general scheme of co-ordination of some of the services of the three constituent bodies of the Chemical Council, probably on the basis of a joint basic annual subscription.

This view was endorsed by the Council and reported to the Chemical Council. It was agreed that further consideration of the recommendations with regard to the improvement and extension of individual services should be deferred until the Chemical Council had considered the possibility of devising such a general co-ordination scheme.

### (3) *Coronation of Their Majesties The King and Queen.*

A loyal and dutiful Address of Congratulation to His Majesty the King, drawn up by the Chemical Council on behalf of the Chemical Society, the Institute of Chemistry and the Society of Chemical Industry, was presented on the occasion of the Coronation of Their Majesties the King and Queen on 12th May.

## VI. ADMINISTRATION.

### (1) *Council.*

*Personnel.*

In April, the Council received with much regret the resignation of Professor G. I. Finch as an Ordinary Member of Council owing to his appointment to the Fondation Francqui Chair at Brussels during the coming academic year. Dr. R. J. W. Le Fèvre was appointed to fill the vacancy until the Annual General Meeting in March 1938.

*Territorial Representation on Council.*

In order to meet the wishes of Fellows expressed through Local Representatives, a scheme for territorial representation on Council has been drawn up. This involves the division of the British Isles into six constituencies, each of which will be entitled to a certain number of representatives on the Council, depending essentially on the number of Fellows resident in each constituency. The main principles of the scheme have been arrived at in consultation with Local Representatives, and substantial agreement has been reached in regard to details.

Further particulars of this scheme and of certain other proposed changes in the constitution of Council will be sent to Fellows, who will be given an opportunity of expressing

their opinion for or against the whole project, for the guidance of the General Meeting to which the recommendations for the corresponding alterations of the Bye-Laws will be submitted.

(2) *Mode of Election of Fellows.*

In the opinion of the Council, the present system for the election of Fellows is unduly cumbrous, and involves unnecessary expenditure of money and time, in that it necessitates that forms of recommendation of candidates shall be published in full in the *Proceedings*, their names must be read at three scientific meetings, and their election effected by ballot by those Fellows attending the last of these meetings. Moreover, as only a very small proportion of Fellows are present at any one scientific meeting, this system of voting is not representative, and in practice the ballot has tended to become a mere formality. It is proposed, therefore, that the ballot should be abolished, and the election of Fellows put in the hands of the Council, but that Fellows should receive prior notice of the names of candidates for election and be given an opportunity of lodging an objection to any of them.

Further particulars of this proposal will be sent to Fellows, who will be enabled to express their opinion for or against the proposal before the corresponding alterations of the Bye-Laws are submitted to a General Meeting.

(3) *Local Representatives.*

During the year, the Council has accepted with much regret the resignations from the office of Local Representative of Mr. D. Ll. Hammick (Oxford) and of Professor W. Wardlaw (Birmingham), and has expressed its high appreciation of the valuable services they have rendered. Mr. R. P. Bell and Dr. Stanley Peat have been appointed to fill the respective vacant places.

A meeting of Local Representatives was held in London on 17th March, and various suggestions were referred to Council for consideration and action.

(4) *Centenary Celebrations, 1941.*

In March 1941 the Society will complete the first hundred years of its existence, and the Council has taken steps to set up a General Committee representative of all phases of the Society's activities and Fellowship to consider arrangements for the celebration of the Centenary.

## VII. FINANCE.

(1) *Accounts.*

*General Purposes Account.*

The excess of expenditure over income amounts to £757 (against £303 in 1936). Income is £122 less than in 1936, owing to a decrease of £87 in Life Composition Fees and of £34 in annual subscriptions. Expenditure increased by £332.

*Publications Fund.*

*Income.* Proceeds from sales of publications and advertisement receipts are up by £410 and £59, respectively. Donations show an increase of £384.

*Expenditure.* The cost of the *Journal* is up by £371, and of the Abstracts by £693. The *Annual Reports* cost £91 less.

*Library Fund.*

The amounts received towards the cost of maintenance of the Library for 1937 were £691 from the Institute of Chemistry, £394 from the Society of Chemical Industry, and £392 from the Chemical Society. In addition, £227 was received from other sources.

The Chemical Society spent £593 on books and periodicals, and £149 on binding; it also provided 97 copies of the *Journal* and 38 copies of the Abstracts "A" for exchange with other Journals.

*Investment.*

A sum of £299 11*s*. 5*d*. out of accumulated Life Composition Fees has been invested in £308 7*s*. 3 per cent. Funding Stock, 1959–69.

(2) *Contributions.*

The following contributions have been received towards the cost of the Society's publications for 1937 :

£700 from the Government Publications Grant (through the Royal Society).
£880 from the Chemical Council.

The following sums have also been received from Fellows in commemoration of their completion of 50 years of Fellowship :

| | |
|---|---|
| Dr. George McGowan ................................ | £10 |
| Dr. Sydney Martineau ................................ | £50 |
| Dr. G. T. Moody ...................................... | £50 |

and have been or will be placed to the Centenary Fund.

The Council expresses its sincere thanks for these welcome contributions.

The Council also records its high appreciation of the generous action of those Fellows who continue each year to subscribe to the Publications Fund.

(3) *Bequests.*

Under the Will of the late Lady Tilden, the residue of her estate, after payment of legacies, annuities, and other expenses, is to be divided equally between the Royal Society and the Chemical Society.

The late Professor A. G. Perkin has bequeathed to the Society one fifth of the residue of his estate after payment of certain life interests.

(4) *Fire Insurance.*

The insurance of the property of the Society against the risk of fire has been increased by £3671.

## VIII. RELATIONS WITH OTHER BODIES.

(1) *Chemical Council.*

Reference has been made above to the principal affairs of the Society in which the Chemical Council has played an important part during the year.

The second Annual Report of the Chemical Council is reproduced in Appendix A.

(2) *Representation of the Society on other Bodies.*

The following Fellows have been appointed to represent the Society :

*Bristol University Court* :
Professor F. G. Donnan.
*British National Committee for Chemistry* :
The President, Treasurer, and Senior Secretary.
*British Standards Institution* :
*Council of the Chemical Division* : Dr. J. J. Fox.
Technical Committees :
Co-ordinating the work of the Divisional Councils in regard to any British Standard which may be issued in future for units, conversion factors, fundamental formulæ, values for properties of materials, etc. : Dr. H. J. T. Ellingham.
Specifications for Materials and Plant used in Electroplating : Dr. U. R. Evans.
Standardisation of Scientific Glassware : Dr. J. J. Fox and Dr. E. B. Hughes.
Standards for use in the Dairying Industry : Mr. A. L. Bacharach and Mr. Eric Voelcker.
Chemical Symbols and Abbreviations : Dr. C. F. Goodeve.
*Bureau of Chemical and Physiological Abstracts* :
Mr. F. P. Dunn, Dr. G. A. R. Kon, Professor R. G. W. Norrish and the Senior Secretary, with the Treasurer *ex-officio*.
*Chemical Council* :
Professor F. G. Donnan, Professor I. M. Heilbron and Sir Gilbert Morgan.

*City and Guilds of London Institute* :
The President.
*Faraday Society* :
Colloid Committee : Mr. D. C. Henry.
*Home Office* :
Air Raid Precautions Department : Mr. J. Davidson Pratt.
*Joint Library Committee* :
Professor H. Bassett, Dr. O. L. Brady, Professor J. W. Cook, Professor C. H. Desch, Mr. M. B. Donald, Professor A. C. G. Egerton, Dr. H. J. Emeléus, Dr. C. F. Goodeve, Professor C. R. Harington, Dr. T. A. Henry, Dr. E. W. McClelland, Dr. W. H. Mills, Dr. E. E. Turner, Dr. J. C. Withers.
*Lawes Agricultural Trust* :
Committee of Management : Dr. E. F. Armstrong.
*Royal Microscopical Society* :
Committee dealing with Standardisation of Biological Stains : Professor A. G. Green.

(3) *Representatives of the Society at Public Functions.*

XVIIth Congrès de Chimie Industrielle and the 20ème Anniversaire de la Fondation de la Société de Chimie Industrielle (Paris, September 26th–October 2nd) : The President and the Treasurer.
Société Chimique de Belgique, Jubilee Celebrations (Brussels, 5–7th June) : Mr. W. A. S. Calder.
University of Durham Centenary Celebrations (Durham, 3rd July) : The President.
Réunion Internationale de Physique et Chimie et Biologie (Paris, 30th September to 7th October) : Professor J. W. Cook.
University of Allahabad 50th Anniversary Celebrations (Allahabad, 16th November) : Sir Bryce C. Burt and Sir Prafulla C. Rây.
University of Liége, Centenary Celebrations of the Foundation of l'Ecole des Mines (Liége, 26th and 27th November) : Professor G. I. Finch.

## IX. ACKNOWLEDGMENTS.

The Council expresses its cordial thanks to those Fellows who have placed their valuable services at the disposal of the Society during the year, including Members of Committees, Local Representatives, Referees of papers submitted for the *Journal*, Contributors to the Annual Reports, and those who have given Lectures, opened Discussions and read papers.

The Council has expressed its high appreciation of the services of Mr. A. J. Greenaway and Professor J. T. Hewitt as representatives of the Society on the Bureau of Chemical Abstracts since 1924 and 1926 respectively.

The thanks of the Council have been conveyed to Mr. A. Bracher, Dr. R. Lessing, Mr. Emile Mond, and Professor S. Sugden for presenting volumes of the Society's publications; to Dr. E. F. Armstrong for various books, papers, etc., of historic interest from the late Professor H. E. Armstrong; to Professor J. B. Leathes for meeting the cost of the sections of Abstracts supplied to him as a Fellow; to Sir Robert Mond for a copy of the bronze medal struck to commemorate the 20th Anniversary Celebrations of the Société de Chimie Industrielle; and to the Wellcome Foundation, Ltd., for a replica of the commemorative medal struck in honour of Dr. F. B. Power.

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## APPENDIX A.

### SECOND ANNUAL REPORT OF THE CHEMICAL COUNCIL.

**6th December, 1937.**

Since the publication of its first Annual Report (2nd December, 1936), the Council has pursued the policy therein outlined of promoting co-operation between the three Chartered Chemical Bodies, and in raising a fund to assist in meeting the cost of chemical publications and the Chemical Library.

The constitution of the Council provided that the object of the fund should be the allocation of grants for the co-ordination of scientific and educational publications, the publication of new discoveries, the promotion of research, the maintenance of the library of the Chemical Society, and eventually the provision of adequate accommodation.

The appeal for the fund was based on the proposal that " Industry " might help in the endeavour to cope with the overwhelming increase in the output of new scientific knowledge, which must be published and may, at any time, become of direct practical importance in the affairs of everyday life.

The Chemical Society (for nearly 100 years) and the Society of Chemical Industry (for nearly 60 years) have published the record of progress of pure and applied chemistry almost entirely at the expense of their members, but, owing to the extraordinary development of the science, those who pursue it have become divided into other specialised societies and groups, so that there are now twenty different bodies, of which British chemists may become members. As a result, the membership of the two large publishing societies has, for some years past, remained nearly stationary, and the societies have found their expenditure exceeding their income.

While universities, colleges and other institutions are often endowed by generous benefactors, with funds for research purposes, provision has seldom been made for the publication of results; yet the importance of such publication to the country is incalculable. Government help is provided by a Publications Grant, administered by the Royal Society, and from that the Chemical Society has received very valuable help, but it must be borne in mind that other sciences also require assistance. It follows, therefore, that if chemical publications are to continue to serve a useful purpose, the cost must still be met largely by chemists themselves. In other words, every chemist, whether he wishes to possess the publications or not, should help in defraying the cost of producing them.

Before the issue of the first appeal, in June 1936, the Council received many contributions and promises from chemists,—including £9000 from Sir Robert Mond (which, being contributed under Deed of Covenant, will ultimately realise approximately £11,491 13*s.* 4*d.*), and a sum of £2128 19*s.* 7*d.* received from the liquidators of the Association of Scientific and Technical Institutions, in respect of contributions previously made by chemists to the funds of that Association.

In the first appeal issued by the Council, it was sought to obtain funds for (*a*) an *endowment* fund to provide permanent additional income for the publications, and (*b*) a *capital* fund to maintain the cost of the library, and (eventually) to provide suitable premises.

However, at the request of the contributors who are members of the Association of British Chemical Manufacturers and of Allied Associations, the greater part of the sum so far promised or contributed is to be devoted to *current expenditure* for the next seven years, in the hope that, with the help of the Council, the societies may be placed on a self-supporting basis and may be able to augment the numerical strength of their membership, by working in closer co-operation, and by improving their publications and services, in the interests of all branches of chemistry. Practically the whole of the contributions for *current expenditure* comes from chemical industry.

Accordingly, it will be seen that the contributions (to 22nd November, 1937) for the *Endowment Fund* amount to £24,680 19*s.* 9*d.* and those for *Current Expenses* to £27,044 18*s.* 9*d.*—in all a sum of £51,725 18*s.* 6*d.* This includes the contributions and promises received in reply to a second appeal, which was published in June, 1937.

The appeals were circulated very widely, but did not meet with that general response for which the Council hoped; in fact, the fund has made good progress through the generosity of comparatively few contributors.

However, it is not for lack of sympathy with, or appreciation of, the objects for which it was established that the number of contributors has been disappointing. The replies contain expressions of encouragement, although in many instances directors or those responsible feel that other causes have a more direct claim upon them. The great City Guilds, for example, indicate that the first call upon their funds must be directed to channels of a strictly charitable nature—such as hospitals, schools, etc.

The banking, railway and insurance companies acknowledge the desirability of promoting the objects of the fund, but do not recognise that science has a direct claim on their consideration. Representative companies in the engineering, electrical, metallurgical, and mining industries, and even some gas companies, suggest that the bearing and importance of chemistry on their undertakings is somewhat remote, notwithstanding that their opera-

tions and the materials they employ are obviously of a chemical nature, and dependent upon chemical science for their development and improvement.

Some companies say that "chemistry is of no direct benefit to us," or that they must limit their financial support to objects more intimately concerned with their own undertakings; others mention that they are already contributing to industrial research associations, and hold that they should restrict their donations to organisations devoted to their own particular industries: such donations should be regarded as their contribution to chemistry. Others consider that it is sufficient that their chemists should subscribe to the societies, or contend that they are supporting chemistry by employing chemists; so that it would seem that they entirely overlook the fact that their chemists are dependent for new scientific and technical knowledge upon the continued existence of the publishing societies. Several manufacturers maintain that, as they possess their own laboratories, and staffs of chemists, it is unnecessary for them to provide funds for the publication of new knowledge discovered elsewhere. It is clear, however, that the work carried out in their laboratories must necessarily be of an *ad hoc* character—work which must have a bearing on their own immediate requirements. They have neither the time or do they wish to run the risk of undertaking fundamental or "long-distance" research, and yet it is upon this kind of research that development depends. Excellent and useful as it is, *ad hoc* research ultimately reaches its limit and the investigator who relies on it will soon find himself at a standstill, owing to the lack of the direction which fundamental enquiry affords.

Notwithstanding these demurs, the effect of which it is sincerely hoped chemists will endeavour to correct, the response referred to above has been very gratifying to the Council, and the publishing societies are now in a position to take steps, without unreasonable restrictions, towards the improvement of their publications. One suggestion in particular, as part of the policy of making the journals of the societies more attractive, for which the Council has already made provision,—namely that each paper accepted for publication should be accompanied by a clear and concise summary of its contents,—has already been adopted. Further than that, it is emphasised that the records of investigations accepted for publication should be of sufficient scientific importance, of wide enough interest, and reasonably complete, and that the subject-matter should be so presented as to render it easily understood.

Among other matters discussed by the Council during the year have been the more even distribution of the cost of publications and the provision of a scheme by which the activities of the Societies can be collated. These are subjects which require careful and thorough investigation, and will be reported upon in due course.

Another problem of immediate urgency which is receiving attention is the housing of the library of the Chemical Society, the accommodation for which at Burlington House, Piccadilly, is now exhausted.

The Chemical Council has had under consideration means for effecting economies in various other directions, and has continued to negotiate contracts for printing and paper supplies. Difficulties arising from reduction of hours in the printing trade, and increase of prices in the paper trade, have had to be met and, in the adverse circumstances, the best terms have been secured.

Since the audit of the accounts (30th September, 1937), funds have been placed at the disposal of both publishing societies.

Professor N. V. Sidgwick, C.B.E., M.A., F.R.S., on completing his term of office as President of the Chemical Society in March last, relinquished his seat on the Chemical Council. The vacancy thus caused was filled by the appointment of the new President of the Society, Professor F. G. Donnan, C.B.E., D.Sc., F.R.S.

The Council acknowledges the further helpful advice of Mr. F. P. Dunn, B.Sc., A.R.C.S., F.I.C., in matters relating to publications, and the continued honorary services of the Registrar and Secretary and the staff of the Institute of Chemistry.

ROBERT H. PICKARD,
*Chairman.*

*30, Russell Square,*
*London, W.C.*1.

SUMMARY OF CONTRIBUTIONS RECEIVED AND PROMISED TO
*30TH SEPTEMBER, 1937.*

| | £ s. d. | £ s. d. | £ s. d. |
|---|---|---|---|
| *Endowment Account.* | | | |
| Received and receivable to date per Balance Sheet : | | | |
| Under Deed of Covenant, 1935–36 ... ... ... ... ... | 404 6 11 | | |
| " " " 1936–37 ... ... ... ... ... | 2,129 0 6 | | |
| | | 2,533 7 5 | |
| Donations, 1935–36 ... ... ... ... ... ... ... ... | 6,041 8 10 | | |
| " 1936–37 ... ... ... ... ... ... ... ... | 1,284 0 3 | | |
| | | 7,325 9 1 | |
| | | | 9,858 16 6 |
| Amounts outstanding : | | | |
| Under Deeds of Covenant ... ... ... ... ... ... | | 13,757 7 6 | |
| Under Promise ... ... ... ... ... ... ... ... | | 633 9 2 | |
| | | | 14,390 16 8 |
| | | | 24,249 13 2 |
| *Building Account.* | | | |
| Received to date per Balance Sheet ... ... ... ... | | 30 0 0 | |
| Amount outstanding under Deed of Covenant ... ... | | 75 0 0 | |
| | | | 105 0 0 |
| *Current Expense Account (Contributions from A.B.C.M. and Allied Associations).* | | | |
| Received to date : | | | |
| Under Deed of Covenant, 1935–36 ... ... ... ... ... | 120 0 0 | | |
| " " " 1936–37 ... ... ... ... ... | 3,434 1 3 | | |
| | | 3,554 1 3 | |
| Donations, 1935–36 ... ... ... ... ... ... ... ... | 205 0 0 | | |
| " 1936–37 ... ... ... ... ... ... ... ... | 2,423 6 0 | | |
| | | 2,628 6 0 | |
| | | 6,182 7 3 | |
| Amount outstanding under : | | | |
| Deeds of Covenant ... ... ... ... ... ... ... ... | 20,484 7 6 | | |
| *Promises* ... ... ... ... ... ... ... ... ... ... | 328 4 0 | | |
| | | 20,812 11 6 | |
| | | | 26,994 18 9 |
| Total ... ... ... ... ... ... ... | | | *£51,349 11 11* |

*A copy of the audited Accounts can be obtained on application to the Hon. Secretary, The Chemical Council, 30, Russell Square, London, W.C. 1.*

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## APPENDIX B.

### REPORT OF THE BUREAU OF CHEMICAL ABSTRACTS FOR 1937.

Six meetings of the Bureau were held during the year.

The Indexing Sub-Committee, and the A III Advisory Sub-Committee also held meetings.

The Bureau wishes to record its very high appreciation of the services rendered by Mr. A. J. Greenaway and Dr. J. T. Hewitt, who retired from the Bureau at the end of 1937 after having served since 1924 and 1926 respectively.

The most important event in the proceedings of the Bureau during the year has been the Agreement between the Physiological Society, the Biochemical Society, the Chemical Society, and the Society of Chemical Industry, dated July 13th, 1937, whereby the Physiological Society becomes one of the constituent members of the Bureau. The title of the Bureau is to be changed to " Bureau of Chemical and Physiological Abstracts," and the production of Physiological Abstracts will be undertaken by the Bureau as a part of Section A III, which will have the new title of " Physiology and Biochemistry."

The first representatives of the Physiological Society on the Bureau are Prof. J. H. Gaddum and Prof. B. A. McSwiney. Prof. Samson Wright has been appointed the first Assistant Editor of the Physiology Section of A III.

A Sub-Committee consisting of the Chairman of the Bureau, Mr. J. L. Baker, Prof. J. H. Gaddum, and Prof. B. A. McSwiney has been appointed in accordance with the Agreement to deal with questions of policy and finance of Section A III.

A junior clerk has been engaged to deal with the additional work due to this new arrangement.

*Abstracts.*—The total number of abstracts published during 1937 was 35,939, as compared with 34,321 in 1936, an increase of 1418. The appended table shows the number of abstracts and pages printed in each quarter, as well as the average length, the figures for 1936 being included for comparison.

| | Abstracts A. | | | | Abstracts B. | | | |
|---|---|---|---|---|---|---|---|---|
| | 1936. | | 1937. | | 1936. | | 1937. | |
| | No. of Abs. | Pages. | No. of Abs. | Pages. | No. of Abs. | Pages. | No. of Abs. | Pages. |
| 1st quarter ...... | 4,464 | 396 | 4,103 | 394 | 3,840 | 286 | 3,925 | 298 |
| 2nd ,, ...... | 4,243 | 372 | 4,998 | 454 | 4,026 | 288 | 4,424 | 328 |
| 3rd ,, ...... | 4,396 | 398 | 4,316 | 398 | 4,386 | 320 | 4,555 | 360 |
| 4th ,, ...... | 4,295 | 406 | 4,122 | 424 | 4,671 | 344 | 5,496 | 428 |
| | 17,398 | 1,572 | 17,539 | 1,670 | 16,923 | 1,238 | 18,400 | 1,414 |
| Average length per abstract ... | 0·18 Column | | 0·19 Column | | 0·15 Column | | 0·15 Column | |

The 17,539 "A" Abstracts comprised 8089 in A I, 3065 in A II and 6385 in A III. The corresponding figures for 1936 were 8236, 3156, and 6006.

Of the 18,400 "B" Abstracts, 10,883 were from journal literature and 7517 were abstracts of Patents (in 1936, 8771 and 8152 respectively).

It will be observed that the total number of "A" Abstracts has increased slightly, but the number of abstracts in Sections A I and II is slightly lower than in 1936, whereas the abstracts in Section A III show an increase of about 5 per cent. in number; this is in accordance with the increasing volume of biochemical literature now being published.

The greatest change in the Abstracts has occurred in Section "B," where it will be seen that, although there was a small decrease in the number of Patents abstracted, the abstracts from journal literature were 2112 more than in 1936. This is due to two main causes. Firstly, many more abstracts are being prepared for the Bureau, particularly by Mr. A. G. Pollard, Mr. R. B. Clarke, and Dr. W. L. Davies, who have used journals available to them at the Science Library, the Fuel Research Station, and the National Institute for Research in Dairying. The second factor has been the receipt by the Bureau of some fifty journals, not previously available, on loan from the Science Library. These journals deal mainly with technical subjects, and the abstracts from them have filled in many gaps which could otherwise only have been done at heavy expense. The loan of these journals has been rendered possible by the very helpful co-operation of Dr. S. C. Bradford, the Librarian of the Science Library, and the Bureau wishes to record its grateful thanks to him for his services, and also to Mr. A. G. Pollard, who has kindly undertaken the task of collecting these journals and forwarding them to the Bureau.

*Annual Index.*—The joint Annual Index to the Abstracts for 1936 covered 794 pages, an increase of 40 pages over the 754 of the 1935 Index. The cost of printing the Index was £1539 7*s.* 11*d.* and of the paper £231 11*s.* 9*d.* (corresponding figures for the 1935 Index were: £1445 19*s.* 9*d.* and £290 8*s.* 3*d.*). The total number of entries in the Index was 113,160, compared with 105,850 in 1935.

*Indexing Department.*—During the year the proposals regarding this section of the work made by the Bureau to the two Societies were formally approved. A number of applications were received for the position of full-time Assistant Indexer, and finally Miss E. M. Tanner was selected; she commenced work on August 1st, and a room was secured at 26, Charing Cross Road, to house the Indexing Department. Although this arrangement has been in operation only for a short time, it appears to be working very satisfactorily.

In order to deal with the increasing bulk of abstracts, and particularly those in Section A III, it has been arranged that Miss Goring Thomas, who has previously given part-time assistance, shall be employed full-time on indexing work during 1938.

*Improvement of Abstracts.*—The Bureau has, at the request of the Chemical Society, considered means whereby improvements could be effected in the " A " Abstracts, and has presented a report to the Chemical Society on the subject.

Consideration is being given to the possiblity of further collaboration with other organisations publishing abstracts.

In order to advise on possible improvements and consider details connected with the Abstracts, the following provisional Advisory Sub-Committees were appointed, and were asked in particular to explore the possibilities of further collaboration as indicated above :

For A I and A II : Dr. H. J. T. Ellingham (*convener*).
Mr. F. P. Dunn
Dr. G. A. R. Kon
Prof. R. G. W. Norrish.

For " B " : Dr. L. A. Jordan (*convener*).
Dr. F. H. Carr
Mr. F. P. Dunn
Mr. W. Macnab.

These two Sub-Committees are in addition to the A III Sub-Committee referred to above.

*Prices of Abstracts.*—A revised scale of prices for the various sections of the Abstracts was presented to the two Societies, and has been approved for adoption in 1938.

*Decennial Index.*—A further 22 copies of the Decennial Index have been sold during the year, making a total of 825.

The further sum of £50 has been forwarded to each of the two Societies as representing half of the available balance in the Decennial Index Fund.

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## APPENDIX C.

### REPORT OF THE JOINT LIBRARY COMMITTEE FOR 1937.

Excluding the evenings on which meetings of the Chemical Society were held, there were 8554 attendances during the year, as compared with 8917 in 1936. Of these 4988 were made by Fellows of the Chemical Society, and 3566 by Members of other Constituent and Contributing Bodies, as against 5377 and 3540 in 1936.

The number of books borrowed was 5666, against 5594 in the previous year; of these 1468 were issued by post, compared with 1650 in the preceding year.

The Library telephone facilities are still extensively used, and the incoming calls included 941 inquiries which necessitated reference to books in the Library, as against 937 the previous year.

The additions to the Library comprise :

> 274 books, of which 87 were presented, 738 volumes of periodicals and 201 pamphlets; as against 257 books, 734 volumes of periodicals and 224 pamphlets last year.

*Analysis.*

| | Attendances. | Books borrowed. | Books. added. | Volumes of periodicals added. | Pamphlets added. |
|---|---|---|---|---|---|
| 1937 ............ | 8554 | 5666 | 274 | 738 | 201 |
| 1936 ............ | 8917 | 5594 | 257 | 734 | 224 |

The total number of volumes added during the year was 1012. The Library now contains 41,678 volumes, consisting of 12,551 books and 29,127 bound volumes of periodicals.

The attendances were adversely affected by the Coronation and the Bus strike.

The Committee wishes to record its grateful appreciation of the gifts received from Fellows and others during the year; these included 14 volumes of historical interest, not already in the Society's collection, presented at the wish of the late Professor T. M. Lowry.

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## APPENDIX D.

### LECTURES AND DISCUSSIONS.

*Lectures held in London.*

4th March, on "Some Problems of Tyrosine Metabolism," by Professor H. S. Raper; 17th March, Seventh Hugo Müller Lecture, entitled "Principles of Distribution of Chemical Elements in Minerals and Rocks," by Professor Dr. V. M. Goldschmidt; 29th April, Haber Memorial Lecture, by Professor J. E. Coates; 28th October, Le Chatelier Memorial Lecture, by Professor C. H. Desch; 18th November, on "Bond Character and Interatomic Distance" by Dr. J. M. Robertson.

*Discussions held in London.*

4th February, on "The Transition State in Reaction Kinetics"; 15th April (Joint Discussion with the London Section of the Society of Chemical Industry), on "Physico-Chemical Problems Involved in Distillation"; 20th May, on "Synthesis and Stereochemistry of Condensed Alicyclic Systems"; 2nd December, on "The Influence of Structure on the Action of Parasiticidal Drugs."

*Lectures held outside London.*

*Birmingham.* At the University, Edgbaston: (Joint meetings with the Birmingham University Chemical Society), 8th March, on "Recent Developments in Surface Action," by Professor E. K. Rideal; 15th March, on "Brazilin," by Professor R. Robinson; 15th November, on "Nucleic Acids," by Professor J. M. Gulland.

*Bristol.* At the University: 4th February, on "The Chemistry of Ascorbic Acid and its Analogues," by Professor E. L. Hirst.

*Edinburgh.* At the Pharmaceutical Society, Edinburgh: 17th March, (Joint meeting with the local sections of the Institute of Chemistry and the Society of Chemical Industry), on "Some Fundamental Laws of Chemical Change," by Professor C. N. Hinshelwood; at the University: 2nd November (Joint meeting with the University of Edinburgh Chemical Society), on "Some Aspects of the Organic Chemistry of Nitrogen," by Professor G. R. Clemo.

*Glasgow.* At the Royal Technical College: 19th February, on "Ionic Migration" by Professor J. Kendall; 22nd October (Joint meeting with the Glasgow Sections of the Institute of Chemistry and the Society of Chemical Industry), on "Systematic Theory of the Liquid State," by Professor J. D. Bernal.

*Leeds.* At the University: 28th January, on "Silicates," by Professor W. L. Bragg; 25th November, on "Enzymes as Chemical Tools," by Professor J. M. Gulland.

*Liverpool.* At the University: 29th January, on "Sesquiterpene Ketones, their Structure and Synthesis," by Professor J. L. Simonsen; 24th February, on "Some Aspects of Modern Analytical Chemistry," by Dr. J. J. Fox; 15th March, on "Mechanism of some Biological Oxidations," by Professor D. Keilin; 2nd November, on "Recent Results in the Study of Free Radicals by Photochemical Methods," by Professor R. G. W. Norrish.

*Manchester.* At the Constitutional Club: 8th January, (Joint meeting with the Manchester Section of the Society of Chemical Industry and the Society of Dyers and Colourists), on "Reaction of Diazosulphonates derived from β-Naphthol-1-sulphonic Acid," by

Professor F. M. Rowe; At the University: 16th February, (Joint meeting with the Manchester University Chemical Society), on "The Biochemical Rôle of the Vitamin-*B* Complex," by Professor R. A. Peters. At the Manchester Central Library: 5th November (Joint meeting with the Society of Chemical Industry, the Institute of Chemistry, the Society of Dyers and Colourists, and the Manchester Literary and Philosophical Society), on "Researches on Rubber and Rubber-like Substances," by Dr. Kurt H. Meyer.

*Newcastle and Durham.* Bedson Lectures at King's College, Newcastle-on-Tyne: 1st February, on "Catalytic Activation of Nitrogen," by Professor M. Polanyi; 5th March, on "The X-Ray Interpretation of Protein Structure," by Dr. W. T. Astbury; 21st May, on "Chemistry in Food Production," by Sir John Russell; 25th October, on "Electron Diffraction and Surface Structure," by Professor G. Ingle Finch; 26th November, on "Chemistry in the Ancient World," by Professor J. R. Partington.

*North Wales.* At the University College, Bangor: (Joint meetings with the University College of N. Wales Chemical Society), 21st January, on "Quantitative Study of Some Gas Reactions," by Professor M. W. Travers; 5th November, on "Exchange between Light and Heavy Hydrogen," by Professor C. K. Ingold.

*Nottingham.* At the University College: 29th October, on "The Biochemistry of the Waxes," by Professor A. C. Chibnall.

*St. Andrews and Dundee.* At the University, St. Andrews: 26th February (Joint meeting with the St. Andrews University Chemical Society), on "Crystallography as a Chemical Tool," by Professor G. M. Bennett.

*Sheffield.* At the University: 19th February, on "The Unravelling of Complex Reactions," by Professor H. M. Dawson; 12th November, on "An Hour Among the Alchemists," by Professor John Read.

*South Wales.* At the University College of Swansea: (Joint meetings with the University College of Swansea Chemical Society); 29th January, on "Recent Progress in Inorganic Chemistry," by Professor W. Wardlaw; 28th October, on "Some Aspects of Electrolytic Oxidation," by Dr. S. Glasstone. At the Technical College, Cardiff: 22nd October (Joint meeting with the Cardiff Technical College Chemical Society), on "The Chemical Exploration of the Stratosphere," by Professor F. A. Paneth.

## INCOME AND EXPENDITURE GENERAL PURPOSES ACCOUNT FOR THE YEAR ENDED 31ST DECEMBER, 1937.

| 1936 £ s. d. | 1936 £ s. d. | *Income.* | 1937 £ s. d. | 1937 £ s. d. |
|---|---|---|---|---|
| | 134 15 8 | To Life Composition Fees (£142 10*s.* 0*d.*), one-third as Income ... ... ... ... ... ... | | 47 10 0 |
| | | " Annual Subscriptions: | | |
| 416 7 6 | | Received in advance, on account of *1937* ... | 1040 13 0 | |
| 7677 8 6 | | " during 1937 " " ... | 7528 10 0 | |
| 845 0 0 | | " " " " 1936 ... | 311 17 0 | |
| 14 0 0 | | " " " " 1935 and previous years ... ... ... ... ... ... | 7 10 0 | |
| 8952 16 0 | | | 8888 10 0 | |
| 350 0 0 | | *Less* amount included in last year's Income, being valuation of *Arrears* as per last Balance Sheet ... ... ... ... ... ... | 320 0 0 | |
| 8602 16 0 | | | 8568 10 0 | |
| 320 0 0 | | *Add Arrears* at date: £491 0*s.* 0*d.* Estimated to realise as per Balance Sheet ... | 320 0 0 | |
| | 8922 16 0 | | | 8888 10 0 |
| | 833 17 5 | " Dividends on Investments ... ... ... ... | | 826 12 4 |
| | 224 18 4 | " *Income Tax recovered* ... ... ... ... ... | | 239 8 4 |
| | 13 12 11 | " Interest on Deposit ... ... ... ... ... ... | | 8 17 0 |
| | 60 18 11 | " Miscellaneous Receipts ... ... ... ... ... | | 57 13 2 |
| | *802 19 10* | " Excess of Expenditure over Income carried to Balance Sheet ... ... ... ... ... ... | | 756 15 6 |
| | £10,493 19 1 | | | £10,825 6 4 |

| 1936 £ s. d. | 1936 £ s. d. | *Expenditure.* | 1937 £ s. d. | 1937 £ s. d. |
|---|---|---|---|---|
| | | By Administration Expenses: | | |
| 1993 13 10 | | Office Salaries and Wages ... ... ... ... | 2105 0 1 | |
| 226 7 6 | | Superannuation ... ... ... ... ... ... | 231 13 0 | |
| 284 4 11 | | House Expenses, etc. (proportion) ... ... | 229 6 10 | |
| 52 10 0 | | Accountants' Charges ... ... ... ... ... | 52 10 0 | |
| 278 9 7 | | Miscellaneous Printing and Stationery (proportion) ... ... ... ... ... ... ... | 297 8 3 | |
| 183 3 8 | | Postages ... ... ... ... ... ... ... ... | 192 13 2 | |
| *51 5 7* | | *Miscellaneous* ... ... ... ... ... ... ... | 61 8 9 | |
| | 3069 15 1 | | | 3170 0 1 |
| | 212 9 4 | " Expenses of Meetings ... ... ... ... ... | | 256 16 6 |
| | 5 5 0 | " Donations ... ... ... ... ... ... ... ... | | 15 5 0 |
| | *5841 19 1* | " *Contribution to* Publications Fund ... ... | | 5962 17 10 |
| | | " Contribution to Library Fund: | | |
| 820 0 9 | | For Fittings, Furniture, Books, Periodicals, and Binding ... ... ... ... ... ... | 542 9 7 | |
| *382 19 10* | | *Proportion of Maintenance* ... ... ... ... | 391 10 9 | |
| — — — | | Balance of cost of maintenance ... ... | 57 4 11 | |
| | 1203 0 7 | | | 991 5 3 |
| | 77 12 4 | " Transfer to Staff Pensions Fund ... ... ... | | 77 17 0 |
| | — — — | " Transfer to Centenary Fund ... ... ... ... | | 200 0 0 |
| | 83 17 8 | " Expenses of Local Representatives ... ... | | *63 4 10* |
| | — — — | " Legal Expenses ... ... ... ... ... ... ... | | 21 12 0 |
| | — — — | " Coronation Decorations ... ... ... ... ... | | 49 18 6 |
| | — — — | " Interest on Bank Overdraft ... ... ... ... | | 16 9 4 |
| | £10,403 19 1 | | | £10,825 6 4 |

### INCOME AND EXPENDITURE ACCOUNTS OF OTHER FUNDS FOR THE YEAR ENDED 31ST DECEMBER, 1937.

#### PUBLICATIONS FUND.

| 1936 £ s. d. | 1936 £ s. d. | *Income.* | 1937 £ s. d. | 1937 £ s. d. |
|---|---|---|---|---|
| | | To Publication Sales (including back numbers): | | |
| 2506 14 4 | | Journals and Proceedings ... ... ... ... | 2793 16 2 | |
| 1878 10 8 | | Abstracts ... ... ... ... ... ... ... ... | 2004 1 2 | |
| 23 15 0 | | Collective Index, Vols. I–VI ... ... ... ... | 31 0 9 | |
| 215 0 0 | | Do. 1923–32 ... ... ... ... | 50 0 0 | |
| 909 3 5 | | Annual Reports on Progress of Chemistry ... | 967 6 5 | |
| 1 5 0 | | Other Publications ... ... ... ... ... ... | 1 0 4 | |
| 6 16 0 | | Cheap sets ... ... ... ... ... ... ... | — — — | |
| | 5437 4 5 | | | 5847 4 10 |
| 660 0 11 | | „ Proceeds of Advertisements ... ... ... ... | 748 18 5 | |
| 196 13 4 | | *Less* Commission ... ... ... ... ... ... | 226 6 0 | |
| | 463 7 7 | | | 522 12 5 |
| | | „ Donations: | | |
| 600 0 0 | | Imperial Chemical Industries, Ltd. ... ... | — — — | |
| 11 15 0 | | Fellows ... ... ... ... ... ... ... ... | 15 19 0 | |
| — — — | | *Chemical Council* ... ... ... ... ... ... | 800 0 0 | |
| — — — | | Do. for Summaries to Papers in Journal ... ... ... ... ... ... | 80 0 0 | |
| | 611 15 0 | | | 895 19 0 |
| | 700 0 0 | „ Government Publications Grant (through the Royal Society) ... ... ... ... ... | | 700 0 0 |
| | 806 19 8 | „ Dividends on Investments ... ... ... ... | | 300 0 0 |
| | 69 6 0 | „ *Income Tax recovered* ... ... ... ... | | 94 17 10 |
| | 5 4 | „ Interest on Deposit ... ... ... ... ... ... | | — — — |
| | 5841 19 1 | „ Transfer from General Purposes Account (the balance of expenditure on publications) ... | | 5962 17 10 |
| | £13,350 16 11 | | | £14,323 11 11 |

| 1936 £ s. d. | 1936 £ s. d. | *Expenditure.* | 1937 £ s. d. | 1937 £ s. d. |
|---|---|---|---|---|
| | | By Expenses on account of Journal: | | |
| 1159 18 9 | | Editorial Salaries ... ... ... ... ... ... | 1160 2 3 | |
| 85 12 6 | | Superannuation ... ... ... ... ... ... | 85 12 6 | |
| 33 1 0 | | Editorial Postages ... ... ... ... ... ... | 33 19 8 | |
| 3316 1 8 | | Printing, Paper, etc. ... ... ... ... ... | 3645 17 2 | |
| 558 13 5 | | *Distribution* ... ... ... ... ... ... ... | 596 8 2 | |
| 343 13 6 | | Authors' Copies ... ... ... ... ... ... | 344 18 7 | |
| 18 11 8 | | Miscellaneous ... ... ... ... ... ... ... | 19 5 4 | |
| | 5515 12 6 | | | 5886 3 8 |
| | | „ Expenses on account of Abstracts: | | |
| 1304 15 4 | | Editorial Salaries ... ... ... ... ... ... | 1323 15 4 | |
| 20 18 10 | | Superannuation ... ... ... ... ... ... | 20 18 10 | |
| 79 19 6 | | *Editorial Postages* ... ... ... ... ... ... | 93 18 2 | |
| 1536 16 10 | | Abstractors' Fees ... ... ... ... ... ... | 1626 3 9 | |
| 3571 4 11 | | Printing, Paper, etc. ... ... ... ... ... | 4044 0 9 | |
| 363 6 1 | | Distribution ... ... ... ... ... ... ... | 416 10 5 | |
| 95 12 6 | | Miscellaneous ... ... ... ... ... ... ... | 139 17 9 | |
| | 6972 14 0 | | | 7665 10 0 |
| | 862 10 5 | „ Annual Reports on the Progress of Chemistry: *Printing and Honoraria* ... ... ... ... | | 771 18 3 |
| | £13,350 16 11 | | | £14,323 11 11 |

**Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1937.**

*LIBRARY.*

| 1936 £ s. d. | 1936 £ s. d. | *Income.* | 1937 £ s. d. | 1937 £ s. d. |
|---|---|---|---|---|
| | | To Contribution for Fittings, Furniture, Books, Periodicals and Binding: | | |
| 820 0 9 | | Transfer from General Purposes Account ... | 542 9 7 | |
| — — — | | Do. Herbert Spencer Bequest ... | 200 0 0 | |
| | 820 0 9 | | | 742 9 7 |
| | | „ Contributions through the *Chemical Council* towards maintenance: | | |
| 382 19 10 | | Chemical Society (transfer from General Purposes Account) ... | 391 10 9 | |
| 646 10 0 | | Institute of Chemistry ... | 691 9 4 | |
| 448 0 0 | | Society of Chemical Industry ... | 394 9 11 | |
| | 1477 9 10 | | | 1477 10 0 |
| | | „ Contributions, etc., received from other sources towards *maintenance:* | | |
| 100 0 0 | | Association of British Chemical Manufacturers ... | 100 0 0 | |
| 21 0 0 | | Biochemical Society ... | 21 0 0 | |
| 15 15 0 | | Faraday Society ... | 15 15 0 | |
| 50 0 0 | | Institute of Brewing ... | 50 0 0 | |
| 10 10 0 | | Society of Dyers and Colourists ... | 10 10 0 | |
| 21 0 0 | | Society of Public Analysts ... | 21 0 0 | |
| 3 0 0 | | Fellows ... | 3 0 0 | |
| 7 10 3 | | Miscellaneous receipts ... | 6 5 9 | |
| | 228 15 3 | | | 227 10 9 |
| | — — — | Balance transferred from General Purposes Account ... | | 57 4 11 |
| | £2526 5 10 | | | £2504 15 3 |

| 1936 £ s. d. | 1936 £ s. d. | *Expenditure.* | 1937 £ s. d. | 1937 £ s. d. |
|---|---|---|---|---|
| 649 3 6 | | By Books and Periodicals * ... | 593 4 10 | |
| 147 13 3 | | „ Binding ... | 149 4 9 | |
| 23 4 0 | | „ Furniture ... | — — — | |
| | 820 0 9 | | | 742 9 7 |
| | | „ Maintenance: | | |
| 1403 2 0 | | *Salaries and Wages* ... | 1451 3 5 | |
| 162 3 0 | | Superannuation of Library Staff ... | 167 1 0 | |
| 39 15 8 | | Printing, Stationery (proportion) ... | 42 9 9 | |
| 14 16 2 | | Postages ... | 15 7 11 | |
| 24 9 5 | | House Expenses (proportion) ... | 25 11 6 | |
| 27 10 1 | | Coal and Lighting (proportion) ... | 25 13 7 | |
| 25 1 3 | | Insurance ... | 25 12 10 | |
| 9 7 6 | | Miscellaneous Expenses ... | 9 6 8 | |
| | 1706 5 1 | | | 1762 5 8 |
| | £2526 5 10 | | | £2504 15 3 |

* Other than those received in exchange.

## Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1937.

### RESEARCH FUND.

| 1936 £ s. d. | Income. | 1937 £ s. d. | 1936 £ s. d. | Expenditure. | 1937 £ s. d. |
|---|---|---|---|---|---|
| 491 4 0 | To Dividends on Investments ... | 480 18 9 | — — — | By Honorarium, Hugo Müller Lecturer ... | 21 0 0 |
| 129 7 10 | „ Income Tax recovered ... | 139 18 10 | 20 0 0 | „ Do. Longstaff Medallist ... | — — — |
| 34 2 0 | „ Repayment of Grants ... | 67 15 9 | 2 0 0 | „ Longstaff Medal ... | — — — |
| 4 0 0 | „ Grants not applied for ... | 31 0 0 | 622 0 0 | „ Grants ... | 644 17 6 |
| 1 7 4 | „ Interest on Deposit ... | 16 2 | 8 8 10 | „ Miscellaneous Expenses ... | 5 15 8 |
| — — — | „ Sale of Apparatus ... | 16 4 10 | 7 12 4 | „ Balance, being Excess of Income over Expenditure, carried to Balance Sheet ... | 65 1 2 |
| £660 1 2 | | £736 14 4 | £660 1 2 | | £736 14 4 |

### SPECIAL PUBLICATIONS FUND.

| 1936 £ s. d. | 1936 £ s. d. | Income. | 1937 £ s. d. | 1937 £ s. d. |
|---|---|---|---|---|
| | | To Sales of Publications: | | |
| 70 0 0 | | Abstract "A" *printed on one side of the paper* ... | — — — | |
| 10 17 6 | | Memorial Lectures, Vol. I. ... | 7 14 0 | |
| 10 9 0 | | Do. Vol. II. ... | 6 4 9 | |
| 9 10 10 | | Do. Vol. III. ... | 7 12 0 | |
| 4 12 0 | | List of Fellows ... | 3 4 0 | |
| 1 19 6 | | Portraits ... | 3 2 6 | |
| 5 1 2 | | Faraday Lectures ... | 7 18 11 | |
| 1 0 0 | | Perkin Memorial Volume ... | 1 0 4 | |
| 1 4 | | Discussion Number ... | — — — | |
| 23 17 7 | | Lecture on "Modern Chemical Nomenclature" ... | 4 | |
| — — — | 137 8 11 | Report on Physico-Chemical Symbols ... | 5 12 0 | 42 8 10 |
| | 74 0 8 | „ Dividend on Investments ... | | 74 0 8 |
| | 2 18 0 | „ Interest on Deposit ... | | 1 14 4 |
| | 52 6 0 | „ Excess of Expenditure over Income carried to Balance Sheet ... | | — — — |
| | £266 13 7 | | | £118 3 10 |

| 1936 £ s. d. | Expenditure. | 1937 £ s. d. |
|---|---|---|
| 67 3 5 | By Production of Abstracts "A" printed on one side of the paper ... | — — — |
| 153 8 1 | „ Do. List of Fellows ... | — — — |
| — — — | „ Do. Report on *Physico-Chemical Symbols* ... | 14 5 9 |
| 15 1 10 | „ Reprints for Memorial Lectures, Vol. IV. ... | — — — |
| 3 4 9 | „ Do. Faraday Lectures, Vol. II. ... | — — — |
| 27 15 6 | „ Do. Lecture on "Modern Chemical Nomenclature" ... | — — — |
| — — — | „ Excess of Income over Expenditure carried to Balance Sheet ... | 103 18 1 |
| £266 13 7 | | £118 3 10 |

INCOME AND EXPENDITURE ACCOUNTS OF OTHER FUNDS FOR THE YEAR ENDED 31ST DECEMBER, 1937.

## SPECIAL LECTURES FUND.

| 1936 £ s. d. | Income. | 1937 £ s. d. |
|---|---|---|
| 40 2 7 | To Dividends on Investments | 39 16 10 |
| 5 4 0 | " Income Tax recovered | 5 9 10 |
| 14 5 | " Interest on Deposit | 9 11 |
| 21 15 10 | " Balance, being Excess of Expenditure over Income, carried to Balance Sheet | — — — |
| £67 16 10 | | £45 16 7 |

| 1936 £ s. d. | Expenditure. | 1937 £ s. d. |
|---|---|---|
| 50 0 0 | By Honoraria | — — — |
| 16 7 6 | " Lecture Expenses | — — — |
| 1 9 4 | " Miscellaneous Expenses | 2 16 0 |
| — — — | " Balance, being Excess of Income over Expenditure, carried to Balance Sheet | 43 0 7 |
| £67 16 10 | | £45 16 7 |

## STAFF PENSIONS FUND.

| 1936 £ s. d. | Income. | 1937 £ s. d. |
|---|---|---|
| 77 12 4 | To Transfer from General Purposes Account | 77 17 0 |
| 38 4 0 | " Dividends on Investments | 37 14 9 |
| 4 3 8 | " Income Tax recovered | 4 8 3 |
| £120 0 0 | | £120 0 0 |

| 1936 £ s. d. | Expenditure. | 1937 £ s. d. |
|---|---|---|
| 120 0 0 | By Pension paid during 1936 | 120 0 0 |
| £120 0 0 | | £120 0 0 |

## THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

| 1936 £ s. d. | Income. | 1937 £ s. d. |
|---|---|---|
| 40 15 0 | To Dividends on Investments | 40 2 5 |
| 11 5 10 | " Income Tax recovered | 11 18 6 |
| 13 0 | " Interest on Deposit | 12 0 |
| 105 12 8 | " Excess of Expenditure over Income carried to Balance Sheet | — — — |
| £158 6 6 | | £52 12 11 |

| 1936 £ s. d. | Expenditure. | 1937 £ s. d. |
|---|---|---|
| 150 0 0 | By Harrison Prize | — — — |
| 6 15 0 | " Harrison Plaque | — — — |
| 1 11 6 | " Miscellaneous Expenses | — — — |
| — — — | " Balance, being Excess of Income over Expenditure, carried to Balance Sheet | 52 12 11 |
| £158 6 6 | | £52 12 11 |

INCOME AND EXPENDITURE ACCOUNTS OF OTHER FUNDS FOR THE YEAR ENDED 31ST DECEMBER, 1937.

## CENTENARY FUND.

| 1936 £ s. d. | *Income.* | 1937 £ s. d. | 1936 £ s. d. | *Expenditure.* | 1937 £ s. d. |
|---|---|---|---|---|---|
| — — — | To Donations ... ... ... | 60 0 0 | — — — | By Excess of Income over Expenditure carried to Balance Sheet ... ... ... | 260 6 9 |
| — — — | " Contribution from General Purposes Account ... ... ... | 200 0 0 | | | |
| — — — | " Interest on Deposit ... ... ... | 6 9 | | | |
| | | £260 6 9 | | | £260 6 9 |

## THE HERBERT SPENCER BEQUEST.

| £ s. d. | | £ s. d. | £ s. d. | | £ s. d. |
|---|---|---|---|---|---|
| — — — | To Interest on Deposit in Post Office Savings Bank ... ... ... | 9 7 6 | 309 3 6 | By Expenditure on Repairs to Premises ... ... ... | — — — |
| 309 3 6 | " Excess of Expenditure over Income carried to Balance Sheet ... ... ... | 190 12 6 | — — — | " Transfer to Library Account for purchase of Books ... ... ... | 200 0 0 |
| £309 3 6 | | £200 0 0 | £309 3 6 | | £200 0 0 |

## THE CHEMICAL SOCIETY.—BALANCE SHEETS, 31st December, 1937.

### GENERAL PURPOSES.

| 1936 £ s. d. | 1936 £ s. d. | *Liabilities.* | 1937 £ s. d. | 1937 £ s. d. |
|---|---|---|---|---|
| | 1,044 1 6 | To Subscriptions received in advance ... | | 863 18 0 |
| | 3,246 5 8 | „ Sundry Creditors (Printing and other Expenses) ... ... ... ... ... ... | | 2,563 16 4 |
| | — — — | „ Donation (*not yet allocated*) ... ... | | 50 0 0 |
| 21,241 9 4 | | „ Excess of Assets over Liabilities as per last Balance Sheet ... ... ... ... | 23,071 0 11 | |
| 302 19 10 | | *Deduct* Excess of Expenditure over Income for Year ... ... ... ... | 756 15 6 | |
| 20,938 9 6 | | | 22,314 5 5 | |
| 1,863 0 0 | | *Add* Transfer from Publication Fund | — — — | |
| 269 11 5 | 23,071 0 11 | „ Life Composition Fees (two-thirds) | 95 0 0 | 22,409 5 5 |
| | 202 3 6 | „ Current Account at Bankers (overdrawn) ... ... ... ... ... ... | | 1,920 1 2 |
| | 931 16 6 | „ Herbert Spencer Bequest, unexpended Balance ... ... ... ... ... | | — — — |
| | — — — | „ Loan, Chemical Council ... ... ... | | 1,200 0 0 |
| | £28,495 8 1 | | | £29,007 0 11 |

| 1936 £ s. d. | *Assets.* | 1937 £ s. d. |
|---|---|---|
| 27,717 5 1 | By Investments as per Schedule (cost or value when acquired) ... ... | 28,016 16 6 |
| 431 6 6 | „ Sundry Debtors ... ... ... ... ... ... ... ... ... ... ... | 547 16 4 |
| 320 0 0 | „ Subscriptions in Arrear, £491 0*s.* 0*d.* Estimated to realise ... ... | 320 0 0 |
| 26 16 6 | „ Cash in hand ... ... ... ... ... ... ... ... ... ... ... | 7 18 8 |
| — — — | „ Stock of Paper ... ... ... ... ... ... ... ... ... ... | 114 9 5 |
| £28,495 8 1 | | £29,007 0 11 |

### PUBLICATIONS FUND.

| 1936 £ s. d. | 1936 £ s. d. | 1936 £ s. d. | | 1937 £ s. d. |
|---|---|---|---|---|
| | 11,350 0 11 | | To Excess of Assets over Liabilities as per last Balance Sheet ... ... ... ... | 9,363 3 10 |
| 1,863 0 0 | | | *Less* Transferred to General Account ... | — — — |
| 123 17 1 | | | „ Uninvested Composition Fees ... | — — — |
| | 1,986 17 1 | 9,363 3 10 | | |
| | | £9,363 3 10 | | £9,363 3 10 |

| 1936 £ s. d. | | 1937 £ s. d. |
|---|---|---|
| 9,363 3 10 | By Investments as per Schedule (cost or value when acquired) ... ... | 9,363 3 10 |
| £9,363 3 10 | | £9,363 3 10 |

### RESEARCH FUND.

| 1936 £ s. d. | 1936 £ s. d. | | 1937 £ s. d. | 1937 £ s. d. |
|---|---|---|---|---|
| | 632 0 0 | To Sundry Creditors ... ... ... ... ... | | 336 7 6 |
| 14,699 6 4 | | „ Excess of Assets over Liabilities as per last Balance Sheet ... ... ... ... | 14,706 18 8 | |
| 7 12 4 | | *Add* Excess of Income over Expenditure for year ... ... ... ... | 65 1 2 | |
| | 14,706 18 8 | | | 14,771 19 10 |
| | £15,338 18 8 | | | £15,108 7 4 |

| 1936 £ s. d. | | 1937 £ s. d. |
|---|---|---|
| 14,675 18 0 | By Investments as per Schedule (cost or value when acquired) ... .. | 14,675 18 0 |
| 663 0 8 | „ Cash at Bank ... ... ... ... ... ... ... ... ... ... ... | 432 9 4 |
| £15,338 18 8 | | £15,108 7 4 |

THE CHEMICAL SOCIETY. BALANCE SHEETS, 31ST DECEMBER, 1937

## SPECIAL PUBLICATIONS FUND.

| 1936 £ s. d. | 1936 £ s. d. | *Liabilities.* | 1937 £ s. d. | 1937 £ s. d. | 1936 £ s. d. | *Assets.* | 1937 £ s. d. |
|---|---|---|---|---|---|---|---|
| | 10 5 0 | To Amount prepaid for 1938 ... ... ... ... | | — — — | 1600 0 0 | By *Investment as per* Schedule (cost or value when acquired) ... ... ... | 1600 0 0 |
| | 174 14 9 | ,, Sundry Creditors ... ... ... ... ... ... | | 7 3 | 525 5 10 | ,, Cash at Bank ... ... ... ... ... ... ... ... ... ... ... ... ... | 444 11 5 |
| 1992 12 1 | | ,, Excess of Assets over Liabilities as per last Balance Sheet ... ... ... ... ... ... | 1940 6 1 | | | | |
| — — — | | *Add* Excess of Income over Expenditure for Year ... ... ... ... ... ... ... ... | 103 18 1 | | | | |
| 52 6 0 | 1940 6 1 | *Less* Excess of Expenditure over Income for Year ... ... ... ... ... ... ... ... | — — — | 2044 4 2 | | | |
| | £2125 5 10 | | | £2044 11 5 | £2125 5 10 | | £2044 11 5 |

## SPECIAL LECTURES FUND.

| 1936 £ s. d. | 1936 £ s. d. | *Liabilities.* | 1937 £ s. d. | 1937 £ s. d. | 1936 £ s. d. | *Assets.* | 1937 £ s. d. |
|---|---|---|---|---|---|---|---|
| — — — | | To Sundry Creditors ... ... ... ... ... ... | | 2 16 0 | 1000 0 0 | By Investment as per Schedule (cost or value when acquired) ... ... ... | 1000 0 0 |
| 1088 8 7 | | ,, Excess of Assets over Liabilities as per last Balance Sheet ... ... ... ... ... ... | 1066 12 9 | | 66 12 9 | ,, Cash at Bank ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 112 9 4 |
| — — — | | *Add* Excess of Income over Expenditure for year ... ... ... ... ... ... ... ... | 43 0 7 | | | | |
| 21 15 10 | 1066 12 9 | *Less* Excess of Expenditure over Income for year ... ... ... ... ... ... ... ... | — — — | 1109 13 4 | | | |
| | £1066 12 9 | | | £1112 9 4 | £1066 12 9 | | £1112 9 4 |

## STAFF PENSIONS FUND.

| 1936 £ s. d. | *Liabilities.* | 1937 £ s. d. | 1936 £ s. d. | *Assets.* | 1937 £ s. d. |
|---|---|---|---|---|---|
| 907 14 0 | To Excess of Assets over Liabilities as per last Balance Sheet ... ... ... | 907 14 0 | 902 13 9 | By Investments as per Schedule (cost or value when acquired) ... ... ... | 902 13 9 |
| | | | 5 0 3 | ,, Cash at Bank ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 5 0 3 |
| £907 14 0 | | £907 14 0 | £907 14 0 | | £907 14 0 |

## THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

| 1936 £ s. d. | 1936 £ s. d. | *Liabilities.* | 1937 £ s. d. | 1937 £ s. d. | 1936 £ s. d. | *Assets.* | 1937 £ s. d. |
|---|---|---|---|---|---|---|---|
| 1269 9 0 | | To Excess of Assets over Liabilities as per last Balance Sheet ... ... ... ... ... ... | 1163 16 4 | | 1101 7 11 | By Investments as per Schedule (cost or value when acquired) ... ... ... | 1101 7 11 |
| | | | | | 62 8 5 | ,, Cash at Bank ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 115 1 4 |
| — — — | | *Add* Excess of Income over Expenditure for year ... ... ... ... ... ... ... ... | 52 12 11 | | | | |
| 105 19 8 | 1163 16 4 | *Less* Excess of Expenditure over Income for year ... ... ... ... ... ... ... ... | — — — | 1216 9 3 | | | |
| | £1163 16 4 | | | £1216 9 3 | £1163 16 4 | | £1216 9 3 |

THE CHEMICAL SOCIETY. BALANCE SHEETS, 31ST DECEMBER, 1937.

## CENTENARY FUND.

| 1936 | *Liabilities.* | 1937 £ s. d. | 1936 | *Assets.* | 1937 £ s. d. |
|---|---|---|---|---|---|
| — | To Excess of Income over Expenditure for the year ... ... ... ... ... ... | 260 6 9 | — | By Cash at Bank ... ... ... ... ... ... ... ... ... ... ... ... ... | 260 6 9 |

## THE HERBERT SPENCER BEQUEST.

| 1936 £ s. d. | £ s. d. | *Liabilities.* | £ s. d. | 1937 £ s. d. | 1936 £ s. d. | *Assets.* | 1937 £ s. d. |
|---|---|---|---|---|---|---|---|
| 1941 0 0 | | To Amount received from the Trustees ... ... ... | | — — — | 931 16 6 | By Cash at Bank ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 231 16 6 |
| — — — | | „ Balance unexpended at 31st December, 1936 ... | 931 16 6 | | — — — | „ Cash on Deposit at Post Office Savings Bank ... ... ... ... ... ... | 509 7 6 |
| 309 3 6 | 931 16 6 | *Less* Excess of Expenditure over Income for the year ... ... ... ... ... ... ... ... ... | 190 12 6 | 741 4 0 | | | |
| | £931 16 6 | | | £741 4 0 | £931 16 6 | | £741 4 0 |

# SCHEDULE OF INVESTMENTS.

## GENERAL PURPOSES.

| *Nominal Details.* | *Cost or Value when Acquired.* £ | s. | d. | *Market Value 31st December, 1937.* £ | s. | d. |
|---|---|---|---|---|---|---|
| £787 London, Midland and Scottish Railway 4% Debenture Stock | 839 | 3 | 7 | 818 | 9 | 7 |
| £1520 14s. 3d. Cardiff Corporation 3% Stock, 1914/54 ... ... ... | 1650 | 0 | 0 | 1444 | 13 | 6 |
| £1400 India 2½% Stock ... ... ... ... ... ... ... ... ... ... | 1316 | 1 | 0 | 938 | 0 | 0 |
| £2400 Bristol Corporation 2½% Debenture Stock, Bristol Dock Account ... ... ... ... ... ... ... ... ... ... ... ... | 2070 | 2 | 0 | 2064 | 0 | 0 |
| £2718 London, Midland and Scottish Railway 4% Preference Stock ... ... ... ... ... ... ... ... ... ... ... ... ... | 3572 | 0 | 4 | 2224 | 13 | 2 |
| £1200 Leeds Corporation 3% Stock ... ... ... ... ... ... ... ... | 1143 | 1 | 0 | 1008 | 0 | 0 |
| £1[illegible]98 6s. 2d. Union of South Africa 3% Stock, 1954/64 ... ... ... | 1067 | 12 | 10 | 1041 | 9 | 11 |
| £1200 London and North Eastern Railway 3% Debenture Stock ... | 1033 | 11 | 0 | 942 | 0 | 0 |
| £700 Canada 3½% Stock, 1930/50 ... ... ... ... ... ... ... ... | 704 | 8 | 6 | 714 | 0 | 0 |
| £2529 6s. 9d. 5% *Conversion Loan*, 1944/64 ... ... ... ... ... | 2446 | 2 | 9 | 2896 | 1 | 10 |
| £1100 5% ditto ditto ditto ... ... ... ... ... | 1045 | 0 | 2 | 1259 | 10 | 0 |
| £600 4% Funding Loan, 1960/90 ... ... ... ... ... ... ... ... | 480 | 0 | 0 | 676 | 10 | 0 |
| £12,926 9s. 0d. 3½% Conversion Stock 1961, or after ... ... ... | 10,350 | 2 | 2 | 13,249 | 12 | 3 |
| £308 7s. 0d. 3% Funding Stock 1959/69 ... ... ... ... ... ... | 299 | 11 | 5 | 301 | 8 | 3 |
| | £28,016 | 16 | 6 | £29,578 | 8 | 6 |

## PUBLICATIONS FUND.

| *Nominal Details.* | *Cost or Value when Acquired.* £ | s. | d. | *Market Value 31st December, 1937.* £ | s. | d. |
|---|---|---|---|---|---|---|
| £5260 19s. 9d. 3½% Conversion Stock, 1961, or after ... ... ... | 3645 | 12 | 8 | 5392 | 10 | 2 |
| £3178 1s. 6d. 5% Conversion Loan, 1944/64 ... ... ... ... ... ... | 3199 | 18 | 7 | 3633 | 3 | 5 |
| £517 P. & O. Steam Navigation Co. Deferred Stock ... ... ... | 2060 | 0 | 0 | 898 | 14 | 0 |
| £608 *London, Midland and Scottish Railway* 4% Guaranteed Stock | 457 | 12 | 7 | 609 | 0 | 7 |
| | £9,363 | 3 | 10 | £10,533 | 8 | 2 |

## RESEARCH FUND.

| *Nominal Details.* | *Value or Cost when Acquired.* £ | s. | d. | *Market Value 31st December, 1937.* £ | s. | d. |
|---|---|---|---|---|---|---|
| £1000 *London* and North Eastern Railway 4% 2nd Guaranteed Stock ... ... ... ... ... ... ... ... ... ... ... ... ... | 1010 | 0 | 0 | 895 | 0 | 0 |
| £1034 Great Western Railway 2½% Debentures ... ... ... ... | 1049 | 15 | 11 | 708 | 5 | 9 |
| £1122 Metropolitan Water Board 3% "B" Stock ... ... ... ... | 1002 | 16 | 9 | 1009 | 16 | 0 |
| £1483 London, Midland and Scottish Railway 4% Debenture Stock | 1508 | 3 | 6 | 1542 | 6 | 5 |
| £806 Victoria 3% Stock, 1929/49 ... ... ... ... ... ... ... | 706 | 6 | 2 | 765 | 14 | 0 |
| £4498 11s. 0d. 5% Conversion Loan, 1944/64 ... ... ... ... ... | 4267 | 4 | 10 | 5150 | 16 | 9 |
| £6311 6s. 10d. 3½% Conversion Stock, 1961, or after ... ... ... | 5131 | 10 | 10 | 6469 | 2 | 6 |
| | £14,675 | 18 | 0 | £16,541 | 1 | 5 |

## SPECIAL PUBLICATIONS FUND.

| | | | | | | |
|---|---|---|---|---|---|---|
| £2115 8s. 10d. 3½% Conversion Stock, 1961, or after ... ... ... | £1600 | 0 | 0 | £2168 | 6 | 6 |

## SPECIAL LECTURES FUND.

| | | | | | | |
|---|---|---|---|---|---|---|
| £1299 9s. 4d. 3½% Conversion Stock, 1961, or after ... ... ... | £1000 | 0 | 0 | £1331 | 19 | 0 |

## STAFF PENSIONS FUND.

| | | | | | | |
|---|---|---|---|---|---|---|
| £683 6s. 1d. 3½% Conversion Stock, 1961, or after ... ... ... ... | 527 | 13 | 9 | 700 | 7 | 9 |
| £371 17s. 1d. 5% Conversion Loan, 1944/64 ... ... ... ... ... | 375 | 0 | 0 | 425 | 15 | 5 |
| | £902 | 13 | 9 | £1126 | 3 | 2 |

## THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

| | | | | | | |
|---|---|---|---|---|---|---|
| £61 15s. 8d. 3½% Conversion Stock, 1961, or after ... ... ... ... | 50 | 1 | 5 | 63 | 6 | 6 |
| £1255 London, Midland and Scottish Railway 4% Debenture Stock | 1051 | 6 | 6 | 1305 | 4 | 0 |
| | £1101 | 7 | 11 | £1368 | 10 | 6 |

I have examined the above Balance Sheets and accompanying Income and Expenditure Accounts with the Books and Vouchers of the Society, and certify them to be in accordance therewith. I have also verified the Balances at the Bankers and the Investments.

23, Queen Victoria Street, E.C. 4.
15th February, 1938.

W. B. Keen.
*Chartered Accountant.*

Approved { George Senter
H. D. K. Drew
H. E. Cox.

## PRESIDENTIAL ADDRESS.

Delivered at the ANNUAL GENERAL MEETING held at the University of Manchester on March 31st, 1938.

By F. G. DONNAN, C.B.E., D.Sc., LL.D., F.R.S.

### *Retrospect and Prospect.*

THERE has probably never been a time when the prospects of chemical science were so splendid as they are to-day. Those who, like myself, began the study of chemistry some forty-seven years ago, are filled with envy of the younger men and the great future of scientific research that lies before them. When I went in 1893 to study organic chemistry under the great Johannes Wislicenus in Leipzig, what I might venture to call the classical period of that science was in a state of high development. Wislicenus was a famous exponent of stereochemical concepts, and I learnt much during the time I spent in his laboratory. I remember proposing to him that I should investigate the action of iodine on the silver salt of hydrazoic acid or azoimide, with the object of obtaining the molecule $N_6$. Very politely but firmly the great man declined to allow me to try this idea. Probably he foresaw damage to his laboratory and the possibility of having to pay my funeral expenses. Whether I was discouraged by this extremely wise decision or whether it was that many of my friends were engaged on research in a certain rival establishment in the same city, I moved in the late summer of 1894 to the laboratory of Wilhelm Ostwald. No doubt a certain eminent authority in England would have regarded this as a *facilis descensus Averni*. However, being a very young man, I went with the lightheartedness of youth and became a physical chemist of the Arrhenius–Ostwald–van 't Hoff school. The young men of to-day can scarcely realise the state of affairs at that period. To many of the excellent Professors of Chemistry, the solution of a quadratic equation was a somewhat mysterious operation, and a $dy/dx$ a thing which by all the rules of algebra should be simplified by cancelling out the d's. Ostwald was regarded by many good and worthy men in this country as a strange sort of mathematical theorist, whereas in reality he was a very excellent and practical experimenter, who made comparatively little use of mathematics. Indeed, if my memory serves me right, in one of his lectures he accomplished the feat of deducing the second law of thermodynamics from the first. The following example may serve to show the stress that Ostwald laid on practical handicraft in his laboratory. Having to measure the e.m.f.'s of certain cells, I asked the laboratory "Diener" for a potentiometer and galvanometer. The answer was that I had to make such things myself; and so indeed it was, though I doubt if my methods of electrical soldering were of an orthodox character. Instead of a galvanometer one constructed Ostwald's form of "capillary" electrometer.

I need scarcely remind you that at that time the early Arrhenius theory of ionisation in aqueous solutions was one of the chief themes of research in Ostwald's laboratory. For my Ph.D. thesis I had to measure colorimetrically the depth of colour of aqueous solutions of violuric acid containing various colourless organic acids. Fortunately for me, the results agreed fairly well with the simple ionic theory, though neither Ostwald nor I knew that a "tautomeric" equilibrium was also involved. I had, of course, to design and make my own colorimeter. Although the fact did not at all agree with the ionic theory of that period, I noticed that sodium chloride measurably affected the colour of a solution of violuric acid. This was a comparatively early example of a "neutral salt" effect. I could not explain it, but was much cheered by a kindly letter from Arrhenius in which he pointed out that he had observed similar neutral salt effects in some of his own investigations.

After completing my work in Ostwald's laboratory, I had the good fortune to be able to spend a year in van 't Hoff's laboratory in Berlin. Those were the days when he was beginning his famous series of investigations on the conditions of formation and stability of the "Stassfurt" salts. It was a great revelation to me to see how by means of comparatively simple experiments and the simple (essentially thermodynamic) theory of heterogeneous equilibria, van 't Hoff was able to trace out the various regions of stability, the

" crystallisation paths," and the invariant points of the systems he was studying, *i.e.*, the chlorides and sulphates of Na, K, Ca and Mg in presence of water.

In those far-off days physical chemistry was a comparatively simple branch of science. It was not very much influenced by the kinetic theory of matter as treated by the theoretical physicists. Ostwald once asserted in his lectures that there were only three men in Europe who understood—or thought they understood—this theory. Hence it was not of any use, and unlikely to be true. Indeed, the only part of theoretical physics that really aided chemistry at that time was thermodynamics. As everybody knows to-day, the thermodynamic theory of homogeneous and heterogeneous physico-chemical equilibrium had been completed by J. Willard Gibbs in 1878. His treatment was, however, too difficult for chemists to understand. Probably very few chemists read the books of Duhem and Planck, though the work of Le Chatelier in France and Helmholtz in Germany had a considerable influence. It was, I think, the writings of van 't Hoff and Nernst's celebrated " Theoretische Chemie " (published in 1893) which first made the majority of chemists realise the value of thermodynamical principles and methods.

The period 1883–1913 might, perhaps, be called the " thermodynamic age " of physical chemistry. The development of the American school by Noyes and Lewis, the famous work on heterogeneous equilibria of Roozeboom, Schreinemakers, and van 't Hoff, Haber's great treatise on the thermodynamics of technical gas reactions and Nernst's discovery of his third law were important landmarks of that period. It is amusing nowadays to recollect certain minor extravagances. Ostwald and some of his followers made a graven image of energy and banished atoms and molecules as fictions of the imagination. Chemical reactions were to be described by a sort of operational calculus with sets of simultaneous equations. I remember a certain meeting of the British Association at which Professor Divers gave an address somewhat in that vein, and how this infuriated Professor Dewar. Ostwald, greatly daring, actually gave a lecture at our Chemical Society in which he explained that atoms and molecules could be dispensed with. I fear that the fellow-countrymen of Dalton were both unconvinced and horrified. It is only fair, however, to mention that at a later period—largely due, I think, to the work of Perrin—Ostwald admitted the existence of atoms and molecules as discontinuities of energy.

We know to-day that Einstein's demonstration of the equivalence of mass and energy fully justifies the view that atoms and molecules are special and very high concentrations of energy, so that, from the point of view of the energy concept alone, Ostwald's final conclusion was a correct one. It is also very interesting to observe that in several recent papers and in his recently pubished " Physical Chemistry " Professor Brönsted seems to have put in a precise, novel, and very elegant form a great deal of what the early " Energetiker " strove to express in a vague and imprecise way.

In spite of the enormous development since 1913 of both fact and theory concerning the intimate nature and structure of atoms and molecules, it is a rather striking fact that the period after the war has witnessed the appearance of a number of extremely valuable and important books dealing with " pure " thermodynamics and its application to chemical science. In support of this statement I need only mention the treatises written by Lewis and Randall, Partington, Schottky, Ulich and Wagner, E. A. Guggenheim, and the previously mentioned work of Brönsted. There is, therefore, some justification for the statement that the study of thermodynamics still remains an important part of the training of the young chemist. Fortunately, or perhaps unfortunately, for him the scene is now rapidly changing—developing would be a better word. It is well known that the science of statistical mechanics founded by Maxwell, Boltzmann, and Gibbs provided a statistical basis for thermodynamic laws. For a long time this " rational " basis of thermodynamics remained a sort of caviar to the chemist. Nowadays, however, modern knowledge concerning the nature and possible states of atoms, ions, and molecules and modern quantum mechanics have transformed the older statistical mechanics and combined with it to produce a great statistical science of physico-chemical equilibrium which transcends and at the same time interprets and illuminates the earlier science of thermodynamics. We are fortunate in having in this country, in the person of Professor R. H. Fowler, the greatest exponent of modern statistical mechanics, though probably not many chemists can

understand and digest his famous book on that subject. Nevertheless the time has already come when modern quantal statistics must become an essential part of the knowledge of the young chemist who aspires to a fundamental grasp of chemical science as it exists to-day.

To those older men who, like myself, have lived through the period 1893—1938, it seems almost unbelievable how the rapid progress of physical discoveries and theories has in many respects revolutionised the science of chemistry. I remember at the Liverpool Meeting of the British Association in 1896 deserting the chemical section to listen to the discussion in the physical section on the then newly discovered Röntgen rays. Soon afterwards came the discovery of the negative electron by J. J. Thomson, the discovery of radioactivity and radium in France, and the famous work on the radioactive transformation of atoms carried out by Rutherford and his collaborators at Montreal and Manchester. These were great discoveries that the chemists of that period could understand, and we realised, perhaps at first a little slowly, that a vast extension of chemistry was in progress. The award to Rutherford of the Nobel prize for *chemistry* showed very clearly what the Swedish Academy of Sciences thought about the matter. It was understandable, I think, that few chemists realised the importance of Planck's discovery of the quantum of action in 1900. The distribution of energy in the spectrum of full radiation seemed to have little to do with chemical science. I remember hearing some of my physicist friends talking in the early years of this century about the new Boltzmann–Planck statistics. Thank goodness, I said to myself, that is mathematical physics and not chemistry !

Important events soon followed, mostly due to Einstein and connected with this mysterious and apparently un-chemical quantum : the theory of the specific heats of solids, the photo-electric effect, the theory of light quanta, and Einstein's photochemical law. It became clear that the blessed science of thermodynamics could not cope with these important new discoveries relating to " individual " events and apparent discontinuities, and that a new physical chemistry was rapidly being created. However, it could still be regarded as very " physical " chemistry by most of the members of this Society, something that need not worry a sound practical chemist. Then came the bolts—or rather stars—from Heaven's brightest blue; the famous papers published in 1913 by Niels Bohr. The mysterious quantum had now invaded the atom, that sacred property of *all* chemists. Writing to Chaptal in 1791, Lavoisier could say (*i.e.*, of his new anti-phlogistic chemistry) " Toute la jeunesse adopte la nouvelle théorie et j'en conclus que la révolution est faite en chimie." One might say the same about Bohr's great discovery of the " quantised " Rutherford–Thomson atom. Soon afterwards came, unhappily, the war and a halt, or at all events a slowing down, of some four to five years' duration in the advance of chemical research. When the last shot was fired in November, 1918, I think there can have been very few who had any conception of what the following twenty years held in store for our science. The rapid advance of the electron theory of the " Rutherford–Bohr " atom under the influence of the earlier quantum theory brought a vast enlightenment concerning the nature and relationships of the elements. Then, when the physicists were still drawing pictures of the orbits of their revolving electrons, two chemists, G. N. Lewis and Irving Langmuir (and one must not forget Kossel), utilised the electron theory, without worrying much about orbits, in a wonderful attack on the fundamental chemical problems of valency and molecular structure. It is related that after Langmuir had given a lecture on this subject in Cambridge, Mrs. Langmuir turned to Rutherford and asked him what he thought about it. " Oh," said Rutherford, " a very interesting lecture on botany." As you all know, this new electronic theory of valency and the chemical bond was expounded in G. N. Lewis' remarkable book, " Valence and the Structure of Atoms and Molecules," published in 1923. I think one may say that this particular and most important period of advance in chemical theory reached a certain culminating point when Sidgwick published in 1927 his famous book on " The Electronic Theory of Valency." I must not of course forget to mention that about this time certain eminent organic chemists in this country, *viz.*, Lapworth, Robert Robinson, and Ingold, were using electronic and similar concepts in an important development of the structure, polarity, and reactivity of organic molecules. So far, however, all this was comparatively simple. After a hard day's work, the tired industrial or professional chemist could sink into his armchair of an evening and read about these

matters without tears. Sterner events were not far off, for in the years 1924—26 came the new atomic theory and the new quantum mechanics, and already in 1927 Heitler and London had begun work on the chemist's molecule. Since that time there has been a correspondingly rapid advance in chemical science. What does our excellent friend, the hardworking industrial or professional chemist (or for that matter any chemist who has left the University for six or seven years), have to encounter now in his armchair? Wave-functions, eigen values, potential energy curves, resonance, etc., etc.! It is not as if he might perchance say to himself, behold I am not a physical chemist but just a decent organic chemist (if that branch of chemistry forms his special study). I fear that this line of defence will not do, for organic chemistry, offering as it does the greatest wealth of material, is rapidly becoming one of the most important fields for the application of modern physical theories.

The advance in both theories and facts is now so rapid and in many respects so novel that it becomes increasingly difficult for a chemist to follow current scientific literature. He has at his disposal, of course, the *Annual Reports* published by this Society, and the excellent *Chemical Reviews* published by the American Chemical Society. Apart from many good textbooks which are now available, I can recommend to him such periodicals as *Die Naturwissenschaften*, *Die Ergebnisse der exakten Wissenschaften*, and *Science Progress*. The most modern branches of physical science of importance to the chemist are treated very fully in the volumes of the "Hand- und Jahrbuch der chemischen Physik," edited by Professors Eucken and Wolf. I hope that the excellent series of monographs begun under the editorship of Professors Mark and Polanyi, and entitled "Die chemische Reaktion," will be continued.

When visiting many years ago the engineering works of Messrs. William Allen & Sons, Bedford, I was very struck with the fact that the famous electrical engineer, Dr. Gustav Kapp, was regularly engaged in giving lectures to the staff on advances in electrical science. I came across a somewhat similar state of affairs when visiting (in 1923) the Research and Development Laboratories of the Bell Telephone Company in New York. I found that Dr. Karl K. Darrow gave regular courses of lectures to the research staff on new developments in physics, especially theoretical physics. A consideration of these matters leads me to make a suggestion which may possibly be regarded as impertinent or unnecessary. The suggestion is this: would it not be a good thing if the larger chemical Companies and Research Associations of this country were to have as permanent members of their staffs some man or men whose duty it was to keep abreast of modern developments in physical and chemical theories and methods, and to impart this knowledge to the workers engaged in experimental research and plant and process development? No doubt much is already done by discussions and colloquia, and by occasional lectures given by outside experts. There may well be room, however, for the work I saw carried out by Dr. Kapp and Dr. Darrow.

I have also another suggestion to make, which I hope will not be resented. The rapid invasion of chemistry during the last twenty years by the new methods and theories of physics has put an extra load on the students and teachers of chemistry at our Universities. I know very well that a considerable proportion of the University teachers of chemistry are well versed in the new advances to which I have referred. But chemists, just like experimental physicists, are essentially experimental philosophers. They carry out research experiments, and are usually much occupied in directing the experimental investigations of groups of young postgraduate students. They cannot be expected to lead the life of a mathematician or theoretical physicist, nor is it in general possible for them to encroach too much on the time of good-natured colleagues in another department. My suggestion is, therefore, that every important University Department of Chemistry should have associated with it, as a member of the staff, a Professor or at least a Reader in Theoretical Chemistry. We all know how extremely fortunate Cambridge is in possessing Professor Lennard-Jones, and I feel sure my former colleagues in the Chemical Department at University College, London, will agree with me that the association of Dr. Eduard Teller with us for a year was of the greatest advantage.

Such a University teacher of theoretical chemistry would be in general what is called a theoretical physicist, although there is no reason why he might not equally well be a chemist

who, owing to his special abilities and temperament, had gradually demonstrated his power of advancing knowledge on the theoretical side. I might mention in this respect that Dr. Teller began life as a chemist, and so, I think, did Professor Tolman. Professor Max Born once told me that his earliest work was in the field of physical chemistry.

The older physical chemistry did not appeal to many chemists of that period, because it was not able to deal effectively with what really interested them, namely the intimate structure of molecules and the real nature of valency. One must admit that this point of view had considerable justification. If you told a "really sound" chemist of those days that the kinetics of a particular reaction showed it to be uni- or bi-molecular, he naturally wondered why you worried about such incidental matters. What he wanted to know was where you got to in the end. If you pointed to the successful study of a particular chemical equilibrium, he probably thought to himself, the poor fellow is talking of some badly chosen chemical reaction that he cannot bring to a finish. In extreme cases, the ionisation of electrolytes was regarded as an unpleasant sort of mass phenomenon that had more to do with electricity than chemistry.

Such objections cannot be lodged against the most modern developments of chemical theory. Although the theoretical physicist of to-day deals with electrons, atoms and molecules in a statistical manner, the results throw light on that intimate "individual" character of the units which has always been one of the main goals of the chemist. Speaking before such an expert audience, I need scarcely remind you how by the study of $X$-ray and electron diffraction, atomic and molecular spectra, Raman effects, dielectric constants and dipole moments, magnetic susceptibilities, unimolecular films on liquids, etc., etc., the sizes and shapes of molecules, their internal dimensions and dynamics, the nature and binding energy of valency bonds, the various types of excited states and energy levels of molecules, ions and atoms, and their essential reactivities and reaction possibilities have been greatly elucidated with the help of modern physical theory.

In the stress which I have laid on certain very modern developments, I sincerely hope that our excellent friends the "synthetic," "classical"—or is it the "real"?—organic chemists will not think I have forgotten them. This great branch of chemical science continues its majestic advance with unfailing vigour. Not only in its own more special field but also in the investigation of substances of biochemical occurrence or importance it can show a progress unequalled in any earlier period. Natural colouring matters and related substances, carbohydrates, complex hydrocarbons, sterols, polynuclear compounds, high molecular polymers and condensation products, vitamins, hormones, phytohormones, and even the prosthetic gronps of certain enzymes—I am not competent to attempt to complete the list. In the field of applied and industrial chemistry equally great advances have been made; new and important dyestuffs, emulsifying, wetting and "levelling" agents, synthetic rubbers, antioxidants and vulcanisation accelerators, modern synthetic resins and "plastics," pesticides, fungicides, new and important chemotherapeutic agents—again I do not attempt to complete the list. Here, doubtless, are great regions of thought and fruitful action where the synthetic organic chemist still roams untroubled as yet by electron drifts and stresses, eigen functions, or waves of probability. I advise him, however, to keep his weather eye very bright and open. The time is rapidly approaching, if indeed it is not already here, when the exponents of modern theory, be it called physical, organic or colloid, will pounce upon his preserves.

In the older period of which I have frequently spoken, the principal advances of inorganic chemistry were derived from the ionic theory, the study of heterogeneous equilibria and the investigation of many inorganic reactions by earlier kinetic methods, including much interesting work on catalysis. Then came the important views of Abegg and Bodländer relating to valency, and the famous work of Werner on "complex" compounds. In recent years there has been a great extension in the knowledge of complex (co-ordination) compounds in which full use has been made of $X$-ray analysis and other modern methods. Thus a great deal of inorganic chemistry has become merged in the general progress of chemical theory relating to valency and molecular structure.

There will always be, I think, a certain marked difference between chemists who are chiefly interested in the laws of phenomena and the generalisation of these laws, and those

others whose main interest lies in the nature and behaviour of particular chemical substances or classes of substances. Perhaps I might be permitted to call the first category the physical chemists "par excellence." Their investigations have resulted in enormous advances during the last twenty years. It would be quite unnecessary for me to go into details when addressing such an expert audience. Anyone who calls to mind such subjects as chemical thermo-kinetics, photochemistry and photo-kinetics, the theory of solutions and solubility, weak and strong electrolytes and ionisation, electrochemistry, adsorption phenomena, heterogeneous catalysis, magneto-chemistry and colloid and "surface" chemistry in all their numerous aspects, will realise at once the truly remarkable advances that have been made in these branches of physical chemistry, all of which existed in a vastly less developed form before the war. This list of topics could, of course, be made much longer and might well include various fields of investigation in which both experimental methods and relevant theories were lacking in the earlier period. I hope that the modest list which I have given will serve to exemplify the interesting point of difference that I desired to make namely that the physical chemist is more interested in the laws of phenomena than in the qualities of specific substances. Be it well understood, however, that I have no wish to make "invidious distinctions between the major and minor prophets." It takes many prophets to make a good chemistry.

Recently I had occasion to read an interesting book by Dr. Alwin Mittasch, whose name is so well known in connection with his work on technical catalysis. It was entitled "Catalysis and Determinism; a Contribution to the Philosophy of Chemistry." Although I failed to see what connection exists between catalysis and the rather awesome subject of determinism, the book raises the interesting and perhaps important question: do chemists have a philosophy? Chemists have usually been regarded as hard-headed robust fellows who deal with real concrete things. No chemist in the 19th century ever bothered his head much about the luminiferous ether because he could not isolate it, *i.e.*, put it in a bottle and shake it. I was brought up in an Irish College founded on an old Scottish tradition, so I had a year of "Logic and Philosophy." I fear I came to the conclusion that philosophers were much like our old friend Paracelsus; each man set up his own system and metaphorically burnt the works of his predecessors. In this connection the words of a witty and learned Professor of Greek come to my mind. "Philosophy," said he, "is a disease like the measles. If you are going to catch it, do it when you are young and get it over early."

This amusing remark has no application to that great plastic and continuously developing philosophy of science, which has in large measure taken the place of the older type of philosophical study. We owe it chiefly to the work of mathematicians, physicists and biologists, amongst whom might be mentioned in relatively recent times de Morgan, Clifford, Huxley, Mach, Karl Pearson, Whitehead, Russell, Smuts, Haldane, Planck, Bohr, and Eddington, though many other names will occur to you. The special Journal *Erkenntnis*, edited by Reichenbach and Carnap, is devoted to this subject. Needless to say, I have no intention of entering into details on the present occasion. I simply want to make a strong plea for the study of the philosophy of science by chemists. In the hard task of understanding modern atomic and molecular theories, which is now imposed on all chemists, I think it is the philosophical background, rather than the formal mathematics, which offers the most difficulty. In this respect I would recommend chemists to read everything that Niels Bohr writes, for to my way of thinking he is the profoundest thinker and leader in the most modern development of physico-chemical thought. If the chemist wants to grasp the meaning of the fundamental statistical concept and the "double personality" of radiation and matter, he cannot do better than follow Bohr. We have to realise that the new scientific philosophy is not to be described in terms of the familiar concepts derived from our age-long experience of the ordinary world, for new things have been discovered which require quite new types of concept and new ways of thinking. This is indeed the essential characteristic of the philosophy of science, namely a fluidity of thought and a courageous adaptability to new concepts demanded by new regions of experimental discovery. The formidable mathematical "techniques" associated with the theory of relativity and modern quantum theory impose heavy tasks on those who aspire to use them. The important thing for the student of chemistry is to be able to survey this mathematical

"apparatus" from without, and to get at the real nature of the physical and chemical ideas and the new outlook which underlies it.

A great and splendid prospect, a land of "rare and refreshing fruit," lies before the chemists of the present day. Every experimental tool and every theory of the physicist are at their disposal, ready to be applied to an ever-increasing wealth of material. Nuclear physics will soon become nuclear chemistry. In the famous days when Rutherford and his collaborators at Manchester were elucidating the transformations of the naturally existing radioactive atoms, he used to call on chemists to take a hand. If that great man were alive to-day, he would be the first to call on us to enter the great and rapidly developing field of nuclear chemistry. This is nothing less than a reconstruction and a re-integration of the whole "material" world, in which matter and energy play equivalent parts.

At the other end of the chain of material existence are the living organism and the living cell. In the study of the phenomena of life lies another of the great prospects of physics and chemistry, perhaps the greatest of all. It may well be that in the development of this investigation science will require to form new concepts and adopt new ways of thinking unknown in the physical and chemical theories of to-day. Many biologists hold this opinion and fail to see in existing physico-chemical science any inkling of the finalistic and holistic concepts which they find indispensable for an adequate description of the phenomena of living organisms. Bohr has said that in the fact of life we may have to accept one of those "irreducibles," like the finite velocity of light and the quantum of action. This is, however, no counsel of despair, for the *phenomena* of life appear in many respects to be amenable to our present concepts and ways of thinking. The wonderful development of complex living organisms on this planet and the things they make and do seem at first sight to contradict the entropy principle of an approach to a more random and more "chaotic" state. This principle applies, however, only to an *isolated* system. Our planet is not an isolated system, so that any decrease of entropy (increase of improbability) associated with the organisation and organising actions of life may be over-compensated by the "running down" or increase of entropy associated with the passage of radiation from the hot sun to the cold earth. Maxwell's celebrated demon could cause a diminution of entropy by sorting out the molecules of oxygen and nitrogen in a flask of air. But if the demon could do this without food and without the constant metabolism of food in his inside, and therefore the constant associated increase of entropy, he would be a super-natural ghost. The living organisms we know are not ghosts, but must take in food and metabolise it. Their "improbable" organisation and actions are indissolubly bound up with a running-down to a more probable state of relatively improbable systems produced by the sun's expenditure of a little of its vast store of highly organised energy.

The application of the existing (and developing) principles and methods of physics and chemistry to the study of the intimate processes occurring in living cells and organisms will constitute for a long time to come the most fruitful method of investigation. It is unnecessary for me to mention the very great advances already made in this field by the combined attack of organic chemistry, physical chemistry, and physics. It is undoubtedly the combination of all three disciplines and techniques which leads to the most sure and rapid progress. We see very striking examples of the effects of such combined work in recent investigations on muscles, nerves, enzymes, proteins, and viruses. The lectures on the "Molecular Architecture of Biological Systems," given by Professor Bernal at the Royal Institution during January and February of this year, are highly significant of what is happening to-day, and still more, of what is going to happen to-morrow. Soon the chromosomes and genes of the biologist will become amenable to similar treatment by the methods of physics and chemistry. Whatever the future may hold in store for the investigators of the phenomena of life, the biologists may rest assured that physicists and chemists will always be ready to adopt new concepts and new modes of thought, should the progress of experimental discovery demand such a re-orientation. In the philosophy of science there are no *a priori* principles and no immutable laws of thought (apart, of course, from the exclusion of logical contradictions). As Weyl has pointed out, the world of science is an open world, ever pointing forward and beyond itself. Just before writing this address, I read that wonderful little new book by Einstein and Infeld, entitled "The Evolution of Physics."

There is not a single symbol or mathematical equation in it, though it traces the gradual development of thought in physical science from Galileo and Newton to Einstein, Bohr, and Schrödinger. I recommend it to every member of this audience as a great lesson in the story of physical science, viewed as a gradual and evolutionary process of the formation of ever wider and more abstract concepts adapted to the progress of discovery and the corresponding refinement of our ways of thinking about and describing the world of physics. For the world of physics is also our world, and whether we be chemists, physicists, or biologists, all science is our science. It is, indeed, this drawing together of what were in former days separate "sciences" that offers the greatest hope and the greatest prospect for the future of our own science of chemistry. Whether it be the chemistry of the atomic nucleus, or that of the atom, ion, molecule, micelle or living cell, progress depends more and more on the friendly and close collaboration of all workers in the great domain of science. Who would have thought fifty years ago that an understanding of atoms and molecules would come to be intimately concerned with the theory of differential equations as developed by the pure mathematician? I do not agree with Sir James Jeans that the great Architect of the Universe is probably a pure mathematician, but all of us must allow the human variety a very respectable place in the sun. The dreamer of logical dreams in the study is as indispensable to-day as the worker of magical spells in the laboratory. Science is no hierarchy or oligarchy, but a free democracy open to all the talents.

## *The Franklin Memorial Lecture.*

# EDWARD CURTIS FRANKLIN.

## March 1st, 1862–February 13th, 1937.

A Memorial Lecture delivered on February 17th, 1938.

By Alexander Findlay, M.A., D.Sc.

With the close of the Crimean War there developed in America one of those periods of crisis, due to industrial depression and financial panic, which, to use the language of the American historian, James Truslow Adams, "have been like the pulsations of a vast heart, pumping inhabitants into our unpeopled spaces." It was, we may hazard the guess, one of these pulsations which, in 1857, carried Thomas Henry Franklin, son of a Philadelphian shoe merchant, to the still undeveloped State of Kansas, where, in 1858, at the newly laid out townsite of Geary City, in Doniphan County, he erected a sawmill on the banks of the Missouri River and made lumber from the cotton-wood, sycamore, elm, oak and walnut trees which flourished abundantly along the creeks and rivers of that county. On June 12th, 1861, the young sawmill owner took to wife Cynthia Ann Curtis, a Missourian by birth, whose family had settled in Doniphan County in 1855; and it was at Geary City, on March 1st, 1862, that their first child, Edward Curtis Franklin, was born. In 1867, the Franklin home was moved to the county town of Doniphan, where Edward grew up into early manhood.

To realise the background of Franklin's life and to understand the structure of the society in which he grew up and which, I believe, exercised an important influence on his whole life and outlook, one has to bear in mind that, until 1854, Kansas was still in the hands of the Indians; and although Doniphan County, in the north-eastern corner of the State, was one of the earliest districts to be organised (in 1855), most of the State of Kansas was, in the sixties and early seventies of last century, still undeveloped, and the caravans passing westward along the California and Oregon trails were still subject to hostile attack on the part of the Indians. The life and conditions under which young Franklin spent his boyhood years were, in fact, those which were so thrillingly described by Fennimore Cooper; and it is, no doubt, to the conditions under which his boyhood was spent that one may attribute Franklin's sometimes noticeable impatience with convention and his preference for the simpler conditions which characterise a frontier society. Franklin always seemed to me, indeed, to carry about with him much of the spirit of the frontier.

Franklin received his early education in the public schools of Doniphan, but his scholastic attainments never bronght him much distinction. His mind worked slowly and he preferred to learn from nature and from making things with his own hands rather than from books. And so, as he himself relates in an autobiographical sketch of his life, he "spent much time in fishing for catfish and 'sunfish'; in swimming in muddy sloughs and in the river; in roaming the hills and bluffs, picking and admiring the beautiful wild flowers, gathering and eating quantities of wild strawberries, raspberries, and blackberries. In the autumn he garnered wild grapes, plums, cherries, gooseberries, crabapples, red and black haws, and pawpaws. Also in the autumn hazelnuts, hickory nuts and black walnuts were harvested and preserved for winter consumption. With the winter came skating and snow sports, trapping and shooting cotton-tails and bobwhites, killing tree squirrels, prairie chickens, wild ducks and, occasionally, a wild goose for sport and for food, and blue jays and crows as nuisances." The keen and joyous interest which Franklin exhibited as a young boy in all outdoor pursuits and activities remained with him throughout the whole of his life.

At the age of fifteen, Franklin was sent to school at Park College, a little Methodist boarding school at Parkville, Missouri, but the dietary offered there was distasteful to him

and quite inadequate to his physical needs, and so, after two months of joyless existence, he ran away.

While the book-learning of the schools does not seem to have appealed to him, Franklin possessed a great natural interest in and curiosity about the things of nature; and, encouraged by a wise and earnest father, he found much delight in collecting fossils from the limestone rocks along the Missouri River and in examining insects and other natural objects under a microscope. Even at an early age, also, Edward Franklin and his younger brother William, who later became professor of physics at the Massachusetts Institute of Technology, employed their time in making electric batteries, Leyden jars and even a fair-sized induction coil, and they dabbled with chemicals in a corner of their father's sawmill office. Later, they erected a telegraph line and became expert in sending and receiving messages in the Morse code, and in 1877, a year after Alexander Bell invented the telephone, the brothers, with the help of their father, made a pair of Bell telephones which they used on their telegraph line. Through all these various activities, Franklin gained some knowledge of physical and chemical science, and he acquired a manual expertness and dexterity which proved of the greatest value to him and to others in later years.

Franklin developed slowly and was long in finding the real bent of his mind and in discovering his true vocation. After running away from Park College, he more or less wasted, as he confesses, the next seven years of his life. From 1880 to 1884, he worked in a drug store at Severance, carrying on at the same time a small job-printing shop, and he found expression for his emotional feelings in playing a cornet in the village band. Through all these varied activities, however, he was slowly beginning to find himself, and, under the stimulus of his brother's example, there at length awakened in him a desire for a university education. In 1884, therefore, at the age of twenty-two, Edward Franklin, with his vague ambitions and his varied but somewhat unorganised knowledge, entered the State University at Lawrence. There he studied Chemistry, Physics, and a variety of other subjects—German, French, Surveying, English, Botany, Meteorology, History of Philosophy, and Mental and Moral Philosophy—and graduated B.S. in 1888. After graduation, Franklin, who had already while an undergraduate proved his worth and value as an instructor, was appointed an assistant in chemistry, and for two years he taught elementary chemistry to students of pharmacy and carried out water and mineral analyses for the Professor of Chemistry, E. H. S. Bailey. He received the degree of M.S. in 1890.

To supplement the somewhat restricted training in chemistry which he had received at the University of Kansas, and to widen his outlook, Franklin accompanied his younger brother to Germany in 1890, and worked for a year in Tiemann's laboratory, and he attended the lectures on elementary and organic chemistry given by Hofmann for the purpose, more especially, of studying that great master's lecture technique. He attended also lectures on the calculus by Max Planck and a course on industrial chemistry, in the expectation that he would thereby have an opportunity of visiting some of the German chemical factories. In this, however, he was disappointed, for the class visited only one factory, a brewery, in the products of which there is no reason to believe Franklin had any great interest. Although there is little evidence in Franklin's own research work that his contact with German chemistry made much impression on him, his visit to Germany gave fullness and richness to his life, and he always looked back with pleasure to the evenings spent at the Opera or at concerts, and to the long tour, made largely on foot, through the Rhineland, Switzerland and South Germany which preceded the period of study in Berlin. His love of German folksongs and music remained with him through life.

On returning to America, Franklin resumed his teaching work at the University of Kansas, but the necessity of prosecuting research and of obtaining a doctor's degree, if he was to achieve success in an academic career, drove him in 1893 to Johns Hopkins University to work under Professor Remsen. The research which he carried out there on the action of *o*- and *m*-diazobenzenesulphonic acids on methyl and ethyl alcohols, gained for him in 1894 the degree of Ph.D., and appointment as associate professor at his old University. There he gave instruction in organic chemistry, mineralogy and crystallography, and assaying.

At the age of thirty-two, Franklin's scientific development was still delayed. He had

Edward Curtis Franklin.
(*After a crayon portrait by Rem Remsen.*)

[*To face p.* 584.

had, it is true, a fairly wide experience in the teaching and practice of chemistry; he had acted for a number of years as an instructor at Kansas University; he had spent the summer of 1886 tramping among the San Juan Mountains in Colorado as an assayer and assistant mineral surveyor to a firm of prospectors; and, for a time, in 1888, he was chemist on a sugar plantation in Louisiana. He followed with interest the advances in chemical and physical science which were being made in England and in Europe, and took delight in exercising his great technical skill in constructing apparatus and in repeating some of the recent experiments. As early as 1895, for instance, he made Dewar tubes out of Liebig condensers, that being the only suitable glass then available in America, and in 1896, he blew *X*-ray tubes for his colleagues in physics. No sooner, moreover, was the discovery of argon announced than Franklin proceeded to prepare a quantity of the gas and to seal it up in Plücker tubes made by himself. His interest in chemistry was clearly very much alive, but he had apparently not yet felt the urge to creative work. There appears little doubt that he himself felt that something was lacking, for he recounts that in 1896, not sure that he had in him the makings of a professor, he obtained leave of absence and accepted a post as chemist and co-manager of a gold mine and mill near Los Quemados, Costa Rica. Not finding this work, however, to his taste, he resumed his teaching work at the University. In the autumn of that year, as we shall see later, the inhibitions were swept away and creative energy released, and for more than thirty years thereafter research work was prosecuted with vigour.

In 1897 Franklin married Effie June Scott, sister of the Kansas Congressman Charles F. Scott, and a student at the University of Kansas. Her affectionate devotion to her husband, her bright intellect, her interest in literature and in music, and her gifts as a pianist created a gracious, cultured and happy home life, of which music was an essential part. Franklin, it is true, laid aside his cornet, but his study door was always left open so that he might enjoy the sound of his wife's playing. There were three children of the marriage, one daughter and two sons, and of these three two are still alive. The elder son was killed in an aeroplane accident in 1928, and Mrs. Franklin died in 1931. After the death of his wife, Franklin continued to live in his home on the Stanford Campus and was there joined by his son-in-law and daughter, Dr. Anna Franklin Barnett, a medical graduate of Stanford University, who has inherited the musical ability of her mother.

In 1898, Franklin was appointed professor of physical chemistry at the University of Kansas, and five years later left that university, rather regretfully, on appointment as associate professor of organic chemistry at Stanford University, California. In 1906 he was appointed to the full professorship. Here at this great University of the west, whose widespread Campus gives a feeling of spaciousness to life and whose noble buildings with their open arches, long colonnades and red-tile roofing inspire one with memories of the ancient Spanish Missions, Franklin worked quietly, happily and persistently until his retirement in 1929; and even after his retirement he retained his office and private laboratory in the chemistry buildings and continued his research work till the end. It was, it is true, at the University of Kansas that Franklin's research activity first came to life, but it was during his long period of residence at Stanford University that he built up the great edifice of ammono-chemistry which has earned for him a foremost place among the chemists of the twentieth century. Although Stanford University was founded only in 1885, it early acquired fame through the eminence of its teachers and their contributions to knowledge; and Franklin found great happiness, mental stimulus and inspiration in the vigorous life of the young University and in the frequent intercourse which he was able to have with his colleagues at the University of California at Berkeley.

During the tenure of his professorship at Stanford University, Franklin spent two years, 1911—13, on leave of absence at Washington, where he acted as Professor of Chemistry and Chief of the Division of Chemistry in the Hygienic Laboratory of the Public Health and Marine Hospital Service. While there he not only continued the research work on which he had been engaged at Stanford, but investigated also the radioactivity of the waters of the hot springs on the Government Reservation at Hot Springs, Arkansas, for whose curative properties high claims were made. The results perhaps were regarded as disappointing, for so small was the amount of radium that, as Franklin put it, the invest-

ment on the part of the Government of twelve hundred and twenty-five dollars would supply, at the price of radium then prevailing, an amount of radium emanation equal to that given off by all the springs on the Reservation.

Franklin had a very wide and varied experience as a teacher and lecturer in general chemistry, qualitative and quantitative analysis, assaying, mineralogy and crystallography, chemistry of sugar, physical chemistry, the history of chemistry and organic chemistry. Himself an accomplished analyst, he inculcated in his students care and accuracy in their analytical work; and in the later stages of their training he stimulated their interest by making them repeat some of the preparations and experiments described in the current literature. Franklin's mechanical skill and manual dexterity, cultivated since boyhood, were a constant source of admiration, and most of the sometimes complicated and delicate glass apparatus which he used in his long series of investigations with liquid ammonia, was made by his own hands. In his practical teaching, therefore, he sought to train his pupils to become expert in the construction of apparatus, in glass-blowing and in all the laboratory arts.

As a lecturer, Franklin occupied a high place. His lectures were well prepared and were presented in a clear and orderly manner, but in language which was informal and conversational. His obvious command of his subject gained at once the respect and confidence of the students and his free and easy " western " manner and his occasional use of apt and expressive slang won their hearts. He sought, also, to give vividness to his lectures by means of numerous and striking experiments, and in the preparation and performance of these his skill as a glass-blower and his manipulative ability often played an important part. Taking Faraday as his example, also, Franklin liked to give lectures to young people, and these were largely exhibitions of glass-blowing and demonstrations of the properties of liquid air. He impressed his audience by taking liquid air in his mouth and blowing out a cloud of frozen vapour, and he sent them away happy with presents of little glass vases or coloured glass rings which he had shown them in the making. In these popular lectures, also, he used a little engine made by his father to show that the boiling liquid air in a tube, if connected with the engine, would make it go as well as the steam from boiling water.

To Franklin, literary composition of any sort, even the writing up of his research work for publication, was never an easy matter, but he laboured at it conscientiously and would sometimes spend a whole day, or more, phrasing and re-phrasing a single page of typescript. He was the author of only one book, " The Nitrogen System of Compounds," in which practically the whole research work of his life is embodied. The writing of this monograph he undertook with no feeling of pleasure, but only as a duty. The manuscript was begun about 1923—4, was rewritten at least half a dozen times and was sent in for publication in 1934. One is not surprised to learn that by that time the work had become a veritable bugbear to him.

During the Great War, Franklin served, in California, as a member of the State Council of Defence, of the Committee on Scientific Research, of the Committee on Occupational Selection, and of the Committee on Inventions. In Washington he was a member of the Advisory Board of the Bureau of Mines, of the Advisory Board of the American University Experiment Station, and of the Advisory Board of the Chemical Warfare Service. He was also physical chemist in the Bureau of Standards and consulting chemist to the Nitrate Division of the Bureau of Ordnance of the Navy, and in all these positions his knowledge, experience and judgment were of great value.

That the great services which Franklin performed to American chemistry were appreciated by the scientific and academic world is shown by the honours of which he was made the recipient. North-western University, Western Reserve University and Wittenberg University conferred honorary degrees upon him; and he was elected a member of the National Academy of Science, of the American Philosophical Society and of the American Academy of Arts and Sciences. In 1910 and in 1914 he was Chairman of the California Section of the American Chemical Society, and in 1923, American chemists conferred on him the highest honour which it was in their power to bestow by electing him President of the American Chemical Society. In 1925 the New York Section of the Society

awarded him the Nichols Medal, and a similar honour was conferred on him by the Chicago Section when they awarded him their Willard Gibbs Medal in 1931. English chemists showed their appreciation of the value of Franklin's contributions to chemistry by electing him an Honorary Fellow of the Chemical Society in 1933.

Apart from his work, Franklin's chief interests were in outdoor life. A child of Nature, he rejoiced in her beauty and her grandeur, and he would lift up his voice to heaven in shouts of joy as he gazed on the great Pacific Ocean or on the impressive beauty of the California scenery. "If you like this, stand up and yell," he would say to his companions as he drove in his car by the side of the Pacific Ocean; and for Franklin the appeal of Nature never weakened. In his younger days, he relates, he was especially fond of mountain climbing, camping, camp cooking, fishing, hunting, travelling and handling pack trains; and in his later years, of driving automobiles. His regret was that he was too old when aeroplane flying became possible; otherwise, flying would have been included in his hobbies.

For many years, a part of almost every summer was spent among the mountains of Colorado and California, and he climbed—in some cases more than once—all the best-known and highest mountains of the West, including Pike's Peak in Colorado, the beautiful Mount Shasta in California, and Mount Rainier in Washington. The certificate of the Sierra Club that he had climbed five or more mountains over 14,000 feet high, was one of his proudest possessions. One can therefore understand that it was with emotion and a feeling of wistful regret that in 1929, on his return journey from South Africa, he viewed at a distance of only thirty or forty miles the majestic Kilimanjaro with its summit rising 19,000 feet into the clear air. It may, perhaps, be mentioned here that the invitation sent to him by the Council of the British Association to visit South Africa in 1929 was one of the marks of appreciation which Franklin valued most.

Franklin's love of an active outdoor life made him hate the idea of growing old, and in his later years he fought a determined rear-guard action with age. His last defiant challenge to old age was offered in the autumn of 1936 when he made, unaccompanied, at the age of 74, a thirteen thousand mile motor car tour across the States from west to east and from north to south, lecturing before many of the local sections of the American Chemical Society. A letter, written to me on January 26th, 1937, and describing his great tour, ended with these sentences: "I left home on the first of September and got back home a few days before Christmas. A few days later I went to bed with a nasty cold from which I have not yet fully recovered. You have not lived long enough yet but some of these days you will find that this getting old is hell." From the torments of this hell he, fortunately, did not have to suffer long, for, after a brief illness due to an attack of coronary thrombosis, he passed peacefully to his rest on February 13th, 1937. Of the closing of a long life full of joyous achievement and goodwill, surely we may gratefully say:

> "Nothing is here for tears, nothing to wail
> Or knock the breast; no weakness, no contempt,
> Dispraise, or blame; nothing but well and fair."

Chemists will remember Edward Franklin for his many valuable contributions to their science, but his friends will always think of him as a great human being. A man of simple heart and with a winning smile, he was modest even to the point of self-depreciation. Sincere and honest, warm-hearted and full of sympathetic understanding, he possessed a genius for friendship. Loving all, he was beloved by all, and converse with him was always a pleasure and frequently an inspiration. He was interested in the activities of life, and his joy was to exchange experiences and to get new impressions; bnt he took little part in the discussion of abstract views—political, philosophical or religious. In politics he was tolerant and non-partisan; in religion agnostic.

It has already been remarked that Franklin's scientific development was long delayed and that he did not enter on his period of active research until he was thirty-five years of age. This fact is really not to be wondered at when one recalls that in Franklin's undergraduate days chemical research was carried out at only a few of the universities of America, and not at all at the University of Kansas. There existed for Franklin, therefore, none of

that guidance in research which is available to the young graduate of the present day and none of the stimulus which comes from association with those who are engaged in the work of original investigation. Viewed in this light, the achievements of Franklin in research are all the more remarkable. The stimulus to research came from one of his students, as is related by Franklin himself. "In the autumn of 1896," wrote Franklin, "Hamilton P. Cady, then an undergraduate and now Professor of Chemistry at the University of Kansas, was working at the regulation course in quantitative analysis. Observing after a time that the young man was becoming bored with his task, the writer, at that time giving instruction in analytical chemistry, proposed to him that he prepare several of the cobaltammine salts and confirm the composition of one or two of them by analysis. Some days later, with a beautifully crystallised specimen of one of these interesting salts in his hand, Cady stated that the ammonia in these and other salts containing ammonia must function in a manner very similar to that of water in salts with water of crystallisation. He suggested furthermore that liquid ammonia would probably be found to resemble water in its physical and chemical properties. As a direct consequence of Cady's suggestion has followed all the work done in this country on liquid ammonia."

Although the greater part of Franklin's research work was of a purely chemical character, his earliest researches, as well as some of his later, were physico-chemical, and we may therefore begin with a brief survey of them.

In ignorance of the work of earlier investigators, the solubility in liquid ammonia of some five hundred different substances, elements, inorganic salts and organic compounds, was investigated, and the solvent power of liquid ammonia was shown to be second only to that of water. The alkali metals dissolve in liquid ammonia to form blue solutions from which the metals may be recovered unchanged, although, in course of time, reaction takes place with production of metal amide and hydrogen. This reaction may extend over weeks or months, but was found to be very greatly accelerated by finely divided platinum and ferric oxide. The alkaline earth metals also dissolve in liquid ammonia, and on evaporation of the solutions, solid ammoniates, such as $Ca,6NH_3$, are obtained. The solvent power of liquid ammonia for salts differs, in some cases, very markedly from that of water. Most nitrites and nitrates are soluble in liquid ammonia, as are also many metal cyanides and iodides, including the iodides of mercury and silver. Fluorides and chlorides are the least soluble of the halides. Many organic compounds, also, are soluble in liquid ammonia, but sulphites, sulphates and carbonates, even of the alkali metals, are insoluble or sparingly soluble.

The differences in the solubility relations of inorganic salts in liquid ammonia and in water are well illustrated by the fact that, when a solution of silver bromide in liquid ammonia is added to a solution of barium nitrate, a precipitate of the octa-ammoniate of barium bromide, $BaBr_2,8NH_3$, is formed. Other metathetic reactions also were found to take place in liquid ammonia just as in aqueous solutions.

Liquid ammonia, like water, was found to be an ionising medium in which not only all soluble inorganic salts but also a great variety of organic substances form conducting solutions. Determinations of the electrical conductance of solutions of a large number of substances were carried out, but only some of the more important results can be referred to here. The successful and accurate determination of the electrical conductance of such solutions, it may be emphasised, was made possible only by Franklin's ingenuity in designing and his skill in constructing the complicated apparatus which the investigation necessitated.

The equivalent conductivity of dilute and moderately dilute solutions of salts, such as potassium iodide, potassium nitrate and sodium nitrate, in liquid ammonia at $-33°$ was found to be greater than the equivalent conductivity in water at the ordinary temperature; but the dilution at which the maximum value of the equivalent conductivity was obtained was much greater in liquid ammonia than in water. The Arrhenius coefficient, moreover, or the degree of ionisation according to the classical theory, was much less in liquid ammonia than in water, a result which was in harmony with the ebullioscopic determinations of Franklin and Kraus. This behaviour, also, was to be expected from the relatively low dielectric constant of liquid ammonia, as determined by Goodwin and Thompson; and

the conclusion was therefore drawn that the high conductivity of liquid ammonia solutions is due to the low viscosity of the solvent and the relatively great mobility of the ions. This conclusion found support in the determinations of the ion velocities which were carried out in a most masterly manner by Franklin and Cady, who, using the moving boundary method, found that the mobilities of potassium ion, silver ion, nitrate ion, etc., in liquid ammonia at $-33°$ are from two-and-a-half to three times as great as in water at 18°. In connection with these determinations it may be noted that Franklin and Cady were probably the first to make use of a boundary which depends not on the presence of a coloured ion but on a difference of refractive index of two solutions, although in the publication of the method they were anticipated by B. D. Steele.

That the high mobility of ions in liquid ammonia is associated with a low viscosity of the solvent was proved by the experiments carried out at a later date in Franklin's laboratory at Stanford University, which showed that the viscosity coefficient of liquid ammonia at $-33{\cdot}4°$ is equal to 0·00254, while the value for water at 18° is 0·01054. It may, however, be noted that the Walden rule, according to which the product $\eta\Lambda_\infty$ is nearly constant for a salt dissolved in a number of different solvents, does not hold in the case of liquid ammonia solutions.

The analogy which had been found to exist between liquid ammonia and water as solvents and ionising media suggested to Franklin that methylamine might be analogous to methyl alcohol in its properties. On testing this suggestion, it was found that, just as methyl alcohol is a better solvent for organic compounds than water is, so methylamine is a better solvent than liquid ammonia, and may perhaps be better even than methyl alcohol. In the case of inorganic salts, however, methylamine is inferior as solvent to liquid ammonia, and therefore greatly inferior to water, and may be ranked with methyl alcohol. In its power of combining with both inorganic and organic compounds, however, it probably exceeds even the most reactive of the other solvents, ammonia.

Methylamine was found also to be a good electrolytic solvent, and on determining the change of equivalent conductivity with dilution of a methylamine solution of silver nitrate a very different behaviour was found from that met with in the case of aqueous solutions. Starting with concentrated solutions of silver nitrate in methylamine, the equivalent conductivity at first increases with dilution, reaches a maximum, then falls to a minimum and thereafter increases again. Other workers, it is true, had obtained equivalent conductivity–dilution curves which rose to a maximum and then fell, but the existence of a minimum followed by a rise in the curve had not hitherto been realised.

In their determinations of the electrical conductance of inorganic salts in liquid ammonia, Franklin and Kraus had shown that the equivalent conductivity of potassium iodide and potassium nitrate increases with dilution, at first rapidly, then more slowly and then again rapidly to its final maximum, but no decrease of equivalent conductivity with dilution was observed. The behaviour of methylamine solutions of silver nitrate, however, led Franklin to determine the equivalent conductivity of a larger range of substances in liquid ammonia, and it was found that solutions of potassium amide, copper nitrate, silver cyanide and certain other salts in liquid ammonia give equivalent conductivity–dilution curves similar to that of silver nitrate in methylamine. Similar types of curve were also found by Franklin in the case of solutions of potassium iodide in liquid sulphur dioxide at different temperatures; and in the case of these solutions Franklin was able to show that after passing through a minimum value the equivalent conductivity increases steadily towards a limiting value at infinite dilution.

The abnormal behaviour of such non-aqueous solutions compared with the behaviour of aqueous solutions depends probably on a number of factors and has been the subject of much study by a number of workers, of whom one may mention C. A. Kraus, one of Franklin's earliest collaborators.

The investigation of the solvent and ionising properties of other amines showed that the simpler primary and secondary amines at room temperature are fair solvents for many salts, but the secondary amines are poorer solvents for inorganic salts than are primary amines. They are also less effective ionising solvents.

Besides a few measurements of the electromotive force of concentration cells in liquid

ammonia, from which it appeared that the E.M.F., as in the case of aqueous solutions, is approximately proportional to the logarithm of the ratio of concentrations, determinations of the specific rotation of a number of compounds in liquid ammonia were carried out under Franklin's direction. Although it was found that optical activity is shown by most of the compounds which are active in aqueous solution, the values of the specific rotation in the two solvents may be very different. This fact was most strikingly illustrated by the behaviour of fructose, which shows no measurable activity either in liquid ammonia, in methylamine or in ethylamine.

In concluding this brief survey of Franklin's physico-chemical researches one may refer to the determinations of the physical properties of liquid ammonia—the boiling point under atmospheric pressure, the heat of vaporisation, the vapour pressure of liquid ammonia at different temperatures down to the triple point of solid, liquid and vapour at $-77{\cdot}9^\circ$ and a pressure of 45·5 mm.—and to the determination of the constants for the molecular depression of the freezing point and the molecular elevation of the boiling point, both of which were found to be abnormally low. These determinations, some of which were carried out at a time when no similar work had been done in America, are a tribute to the ingenuity and manipulative skill of Franklin and of the collaborators whom he trained. For accuracy their determinations have remained unsurpassed down to the present day.

The striking parallelism between the general physico-chemical properties of liquid ammonia and water, which had been demonstrated by the earlier investigations of Franklin and Cady and Franklin and Kraus, led to a consideration of the chemical behaviour of derivatives of water and of derivatives of ammonia.

Solutions of ammonium salts in liquid ammonia were found by Franklin and his co-workers to act on sodium, lithium and other metals with formation of salts of the metals and evolution of hydrogen, and they reacted also with insoluble metal oxides and hydroxides in accordance with the equations :

$$NaOH + NH_4Cl = NaCl + H_2O + NH_3$$
$$CaO + 2NH_4NO_3 = Ca(NO_3)_2 + H_2O + 2NH_3$$

just as the aqueous solutions of hydrochloric or nitric acid act on a base insoluble in water. Solutions of ammonium salts in liquid ammonia, also, gave colour changes with phenolphthalein, carmine, safranine, etc., similar to those given by aqueous solutions of acids. It appeared, therefore, from these experiments that the ammonium salts in liquid ammonia solution act as acids.

From their early experiments, which in part confirmed and in part greatly extended the much earlier work of Divers, Franklin and his collaborators were led to an exhaustive examination of the parallelism between the chemical behaviour of derivatives of ammonia dissolved in liquid ammonia and the behaviour of derivatives of water, aquo-compounds as Franklin called them, in aqueous solution. The investigation of the behaviour of the former class of compounds, the ammono-compounds, to use Franklin's nomenclature, constitutes the chief and most characteristic contribution of Franklin to chemistry.

Just as it is assumed that water is ionised in accordance with the equations

$$2H_2O \rightleftarrows (H{\cdot}H_2O)^{\cdot} + OH' \rightleftarrows (H_3O)^{\cdot} + OH'$$
$$\upharpoonleft\downharpoonright$$
$$H^{\cdot} + H_2O$$

so liquid ammonia may be regarded as being ionised in accordance with the equations

$$2NH_3 \rightleftharpoons (H{\cdot}NH_3)^{\cdot} + NH_2' \rightleftharpoons NH_4^{\cdot} + NH_2'$$
$$\upharpoonleft\downharpoonright$$
$$H^{\cdot} + NH_3$$

(Parenthetically, it may be noted that the idea that the ammonium ion in liquid ammonia is an ammoniated hydrogen ion and can act, to use the language of modern theory, as a

proton donor, led Franklin to suggest, by analogy, the presence in water of the oxonium or hydrated hydrogen ion, long before the same suggestion was made by Fajans.)

In accordance with the above schemes, the ions $NH_4^{\cdot}$ and $NH_2'$ in liquid ammonia correspond with the ions $H_3O^{\cdot}$ and $OH'$ in water; and substances, therefore, which dissolve in liquid ammonia to give the ammonium ion may be called ammono-acids, and those substances which give rise to the $NH_2$-ion may be called ammono-alkalis or ammono-bases. The ammono-acids, moreover, react with the ammono-bases in liquid ammonia solution in a manner analogous to the familiar reaction between oxygen acids and bases in aqueous solution.

When one regards the matter from the purely formal chemical point of view, it will be seen that a basic hydroxide may be considered as derived from water by the replacement of one atom of hydrogen by metal (*e.g.*, KOH), and a basic oxide by the replacement of both atoms of hydrogen by metal (*e.g.*, CaO). An oxygen acid, on the other hand, may be regarded as formed by the replacement of one hydrogen atom by an electronegative element or group (*e.g.*, $HO{\cdot}NO_2$) and an acid anhydride by the replacement of both hydrogen atoms (*e.g.*, $NO_2{\cdot}O{\cdot}NO_2$). Finally, an oxygen salt is obtained when one hydrogen atom of water is replaced by a metal and the other by an electronegative element or group (*e.g.*, $K{\cdot}O{\cdot}NO_2$). If, now, one accepts the parallelism between liquid ammonia and water, one may then say that the metallic amides and imides (*e.g.*, $LiNH_2$, $Li_2NH$), which are related to ammonia in the same way as the metallic hydroxides are related to water, may be regarded as bases of the nitrogen system (ammono-bases), while the metallic nitrides are basic nitrides corresponding to the basic oxides of the oxygen system of compounds. On the other hand, the amides of the electronegative elements or groups and also their partly deammonated * products are acids of the nitrogen system (ammono-acids), while the final deammonated products, the acid nitrides, are the nitrogen analogues of the acid anhydrides. Thus, guanidine, $(NH_2)_2C{:}NH$, the analogue of carbonic acid, $(HO)_2C{:}O$, and also cyanamide, $NH_2{\cdot}C{:}N$, and dicyanimide, $HN(CN)_2$, are ammono-acids, and carbonic nitride, $C_3N_4$, is an acid anammonide, analogous to carbon dioxide or carbonic anhydride. In a like manner, potassium acetamidine, $CH_3{\cdot}C({:}NH){\cdot}NHK$, corresponds to potassium acetate, and potassium azide, $KNN_2$, to potassium nitrate.

That these analogies are not merely formal but correspond to something real has, as we shall see, been amply established by the study of the chemical behaviour of the nitrogen or ammono-compounds. Moreover, the validity of the classification of the metal derivatives of the ammono-acids as true salts receives support from the fact that the alkali metal salts of an ammono-acid, in liquid ammonia solution, are much better conductors of the electric current than the acid itself, just as in aqueous solution the alkali salts of acids such as acetic acid are better conductors than the acids.

In order that we may realise the many analogies which exist between the behaviour of the aquo-compounds, or compounds of the water type, when dissolved in water, and the ammono-compounds, or compounds of the ammonia type, when dissolved in liquid ammonia, some at least of the many reactions studied by Franklin and his pupils will now be considered.

According to the Franklin classification, the metal amides and imides are ammono-bases and the analogues of the metal hydroxides. In liquid ammonia solution, therefore, they should behave analogously to metal hydroxides in aqueous solution. Moreover, ammonium salts in liquid ammonia solution are, as has been pointed out, the analogues of the strong acids in aqueous solution. Consequently, just as, in aqueous solution, the base potassium hydroxide reacts with an acid to form a salt and water, *e.g.*,

$$HNO_3 + KOH = KNO_3 + H_2O$$

or

$$(H{\cdot}H_2O)^{\cdot} + OH' = 2H_2O$$

so, in liquid ammonia solution, potassium amide reacts with ammonium nitrate to form potassium nitrate and ammonia:

$$NH_4NO_3 + KNH_2 = KNO_3 + 2NH_3$$

or

$$(H{\cdot}NH_3)^{\cdot} + NH_2' = 2NH_3$$

* The term " deammonation " is used as the analogue of " dehydration."

Other reactions of the same character are represented by the equations: $NH_4NO_3 + AgNH_2 = AgNO_3 + 2NH_3$; $2NH_4I + PbNH = PbI_2 + 3NH_3$; $3NH_4I + BiN = BiI_3 + 4NH_3$. The last reaction is, of course, analogous to the reaction between an acid and a metal oxide. The neutralisation of an ammono-acid by an ammono-base is also illustrated by the reaction, in liquid ammonia, between potassium amide and cyanamide, which is the nitrogen analogue of carbonic acid, to form potassium cyanamide and ammonia: $2KNH_2 + H_2CN_2 = K_2CN_2 + 2NH_3$. This reaction is analogous to that between potassium hydroxide and carbonic acid in aqueous solution.

Since many metallic hydroxides or oxides are precipitated from aqueous solution by the action of potassium or sodium hydroxide on salts of the metals, one was led to expect that metallic amides, imides and nitrides should be precipitated from liquid ammonia solution by the action of potassium amide. Experiment showed that this expectation was entirely justified, reaction taking place as indicated by the following typical equations,

$$AgNO_3 + KNH_2 = AgNH_2 + KNO_3$$
$$PbI_2 + 2KNH_2 = PbNH + 2KI + NH_3$$
$$3HgI_2 + 6KNH_2 = Hg_3N_2 + 6KI + 4NH_3$$

These reactions are a very striking confirmation of the parallelism between the behaviour of the aquo- and the ammono-bases, and the parallelism extends also to the amphoteric properties of certain metal amides. Just as zinc hydroxide dissolves in an aqueous solution of potassium hydroxide to form potassium zincate, so potassium amide in liquid ammonia solution was found to act on zinc amide with the production of a crystalline compound which must be regarded as an ammonozincate of potassium, formed in accordance with the equation, $Zn(NH_2)_2 + 2KNH_2 = Zn(NHK)_2 + 2NH_3$. The ammonozincate was obtained in a beautifully crystalline form containing "ammonia of crystallisation," and had the composition $Zn(NHK)_2,2NH_3$. Investigation showed that a large number of other amides, including those of such strongly positive metals as magnesium, barium, strontium, calcium and even sodium and lithium, react with potassium amide to form compounds which must be looked upon as salts in which these metals play a part closely similar to that which zinc plays in potassium zincate, or which lead and aluminium play in the compounds formed by the action of aqueous potassium hydroxide on the hydroxides of these metals.

In pursuing the investigation of the analogy between water and liquid ammonia, one is led to ask whether, in the case of liquid ammonia, reactions can take place analogous to the hydrolysis of salts by water, with production of basic salts. To this question Franklin obtained by experiment an affirmative answer. Just as aquobasic salts may be produced by the hydrolysis of salts by water, so the analogous ammonobasic salts can be formed by the ammonolysis of salts by ammonia. Thus, lead iodide is ammonolysed by liquid ammonia to form the ammonobasic lead iodide, $PbN{\cdot}PbI,2NH_3$ or $Pb_3N_2,PbI_2,4NH_3$; and many other salts were found to behave in a similar manner. On the strength of these investigations, Franklin discarded the view put forward by Rammelsberg and supported in more recent times by Pesci and by K. A. Hofmann, that all the mercury ammonia compounds are to be regarded as derivatives of so-called dimercuriammonium hydroxide, $Hg_2NOH$. According to this view, the so-called fusible and infusible white precipitates are regarded as double salts of dimercuriammonium chloride and ammonium chloride and represented by the formulæ $Hg_2NCl,3NH_4Cl$ and $Hg_2NCl,NH_4Cl$. These views Franklin considered to be erroneous and without adequate foundation in experimental fact; and he advocated a modified and extended form of the amide theory put forward by Kane in 1839. In agreement with Kane's views, Franklin was able to show that all the mercury ammonia compounds can be regarded as (1) normal mercuric salts with "ammonia of crystallisation," (2) ammonobasic mercuric salts, (3) mixed aquo-ammono-basic salts.

Just as water forms with salts compounds known as salt hydrates or salts with water of crystallisation, so ammonia can form analogous compounds, salt ammoniates or salts with ammonia of crystallisation, in which the combination of the ammonia with the salts is due, as in the case of water, to co-ordination. Quite a number of ammoniated mercuric salts are known, *e.g.*, $HgCl_2,2NH_3$; $HgI_2,2NH_3$; etc., which are formed by the action of ammonia on the mercuric salts. These salts, like the salt hydrates, show a certain vapour

pressure; and the ammoniated mercuric iodide shows the phenomenon of efflorescence when exposed to the air, the colourless ammoniated crystals passing, through loss of ammonia, into the scarlet mercuric iodide, $HgI_2$.

Moreover, when mercuric chloride and liquid ammonia are brought together, part of the salt undergoes ammonolysis in accordance with the equation, $HgCl_2 + NH_3 = NH_2HgCl + HCl$, to form an ammonobasic mercuric chloride. This ammonobasic salt is identical with the long-known infusible white precipitate, the analogy between which and an ordinary basic salt was first pointed out by Kane.

Just as the hydrolysis of a salt is prevented or reduced by the addition of free acid, so the ammonolysis of mercuric chloride can be prevented by the presence of ammonium chloride, which, as we have seen, functions as an acid. Thus, when ammonia is added to an aqueous solution * of mercuric chloride, a precipitate of ammoniated mercuric chloride, $HgCl_2,2NH_3$, identical with the compound known as fusible white precipitate, is formed, provided ammonium chloride is present in sufficient concentration to prevent ammonolysis. If, however, the concentration of ammonium chloride is reduced, ammonolysis of the mercuric salt takes place and the ammoniated mercuric chloride is converted into the ammonobasic salt, $NH_2{\cdot}HgCl$.

When this sparingly soluble ammonobasic mercuric chloride is subjected to the prolonged action of water, it is converted into a substance known as the chloride of Millon's base, a substance which may be regarded as a mixed aquobasic ammonobasic salt, formed in accordance with the equation:

$$2NH_2{\cdot}HgCl + H_2O = HO{\cdot}Hg{\cdot}NH{\cdot}HgCl + NH_3 + HCl$$

This compound is converted by digestion with ammonium chloride solution into the ammoniated mercuric chloride, just as an aquobasic salt is converted into the normal salt by digestion with acid.

The success which attended the classification of inorganic nitrogen compounds as ammono-compounds bearing the same relation to ammonia as the oxygen compounds bear to water, led Franklin to extend his classification to the nitrogen compounds of organic chemistry, and to seek experimental support for it in the preparation and properties of a number of different groups of compounds. Just as ordinary carbonic acid (or aquo-carbonic acid) and carbon dioxide may be regarded as derived from orthocarbonic acid by a process of dehydration, so, argued Franklin, guanidine, $HN{=}C(NH_2)_2$, biguanidine, cyanamide, dicyanimide, dicyanodiamide, melamine, melam, melon, and hydromelonic acid constitute a group of compounds which may be looked upon as ammono-carbonic acids derived by a process of de-ammonation from $C(NH_2)_4$, the hypothetical analogue of orthocarbonic acid. The last member of the group would be carbonic nitride, $C_3N_2$, the analogue of carbon dioxide. Experiment showed that Franklin's surmise was correct, for although guanidine and biguanidine, in aqueous solution, show no acid properties, they and all the other compounds of the above series behave, in liquid ammonia solution, as acids—some weak, some strong—and react in liquid ammonia solution with metal amides to form salts. Thus, when guanidine nitrate in liquid ammonia solution is acted on by potassium amide, dipotassium guanidine is formed: $HN{:}C(NH_2)_2,HNO_3 + 3KNH_2 = HN{:}C(NHK)_2 + KNO_3 + 3NH_3$. Moreover, if guanidine, for example, is an acid in liquid ammonia solution, then its alkyl and aryl derivatives must be regarded as esters and therefore should be capable of undergoing ammonolysis. This was, in fact, found to be the case, reaction taking place according to the equation: $C_6H_5{\cdot}N{:}C(NH{\cdot}C_6H_5)_2 + 3NH_3 = HN{:}C(NH_2)_2 + 3C_6H_5{\cdot}NH_2$. Similarly, salts and esters of cyanamide, dicyandiamide, dicyanimide and other compounds of the series of ammono-carbonic acids have been prepared.

Besides the ammono-carbonic acids derived from the hypothetical $C(NH_2)_4$, Franklin pointed out that the oxygen-nitrogen compounds, cyanic acid, carbamic acid and urea, are, on the basis of his classification, to be regarded as aquo-ammono-carbonic acids,

* Since ammonobasic mercuric chloride, unlike most ammonobasic salts, is not readily decomposed by water, it can be formed by the action of ammonia on mercuric chloride even in aqueous solution.

the last two, for example, being formed by the partial ammonolysis of aquo-carbonic acid, as indicated by the scheme:

$$OC(OH)_2 \xrightarrow[-H_2O]{+NH_3} OC(NH_2)\cdot OH \xrightarrow[-H_2O]{+NH_3} OC(NH_2)_2$$

Although urea, for example, is neutral or very slightly alkaline in aqueous solution, it reacts in liquid ammonia with the alkali metals and magnesium with the evolution of hydrogen, and with potassium amide to form mono- and di-potassium salts. Esters of urea, *e.g.*, ethylurea, diphenylurea, etc., are to be regarded as esters of an aquo-ammono-carbonic acid, which undergo ammonolysis to urea and an amine.

Further, one may regard allophanic acid ($HO\cdot CO\cdot NH\cdot CO\cdot NH_2$), biuret ($NH_2\cdot CO\cdot NH\cdot CO\cdot NH_2$), guanylurea [$NH_2\cdot CO\cdot NH\cdot C(NH)\cdot NH_2$], cyanurea ($NH_2\cdot CO\cdot NH\cdot CN$), etc., as aquo-ammono-dicarbonic acids; and the properties of these compounds are in harmony with this view.

The analogies which were thus, for the first time, emphasised and logically pursued by Franklin inspired a large amount of experimental investigation and enabled a large body of organic nitrogen compounds to be regarded, from one widely-embracing point of view, as the analogues of alcohols, ethers, esters, aldehydes, ketones, carboxylic acids, etc., derived from ammonia in the same way as these oxygen compounds may be regarded as being derived from water. Thus, methylamine, ethylamine, etc., are to be regarded as ammono-alcohols, and the analogues of methyl and ethyl alcohol, etc.; while trimethylamine is to be regarded as the ammonia analogue of dimethyl ether, and therefore is to be regarded as an ammono-ether. Further, it was found by Franklin and his collaborators that, when acetophenone is heated in liquid ammonia solution, ammonolysis takes place with production of an ammono-ketone, acetophenoneimine, according to the equation, $C_6H_5\cdot CO\cdot CH_3 + NH_3 = C_6H_5\cdot C(:NH)\cdot CH_3 + H_2O$; and a similar reaction takes place in the case of benzophenone. Moreover, when a liquid ammonia solution of ammonium acetate and ammonium chloride is heated, ammonolysis of aquo-acetic acid takes place with formation of ammono-acetic acid, or acetamidine, $CH_3\cdot C(NH)\cdot NH_2$, the nitrogen analogue of acetic acid. From this compound one may expect formation of an ammono-ester, *e.g.*, $CH_3\cdot C(NH)\cdot NH\cdot CH_3$, by the action of methylamine on acetamidine, just as methyl alcohol yields an ester with acetic acid. Experiment fulfilled one's expectation. The formation and chemical behaviour of a large number of nitrogen analogues of organic oxygen compounds were studied by Franklin and his pupils, and the analogies between the two classes of compounds were found to be not merely formal but to extend also to the chemical behaviour of the compounds.

It will be clear that, if there is validity in the analogy between liquid ammonia and water and between the nitrogen compounds and the oxygen compounds, as experiment has, in fact, shown to be the case, then it is to be expected that corresponding to the processes of oxidation one will also find processes of nitridation; and just as oxidation may involve not merely the combining with oxygen but the loss of electrons, so nitridation also may involve loss of electrons. For the terms oxidation and nitridation used in the wider sense, Franklin suggested the term augmentation.

Nitridation or augmentation may be carried out in liquid ammonia solution by various substances, such as hydrazoic acid, iodamine and certain heavy metal amides, imides and nitrides, by reactions which closely resemble those taking place when nitric acid, hypoiodous acid and the heavy metal hydroxides and oxides, the oxygen analogues of the above compounds, act as oxidising agents. Accepting the view first stated by Turrentine, that hydrazoic acid may be regarded as ammono-nitric acid, nitridation or augmentation by hydrazoic acid, *e.g.*, formation of guanidine by heating methylamine with an excess of ammonium azide in liquid ammonia solution, can be considered as analogous to the process of oxidation by nitric acid.

There is no need further to multiply examples of or to discuss in detail the numerous nitrogen compounds which Franklin and his pupils studied and which he showed could be regarded as the nitrogen analogues of the different groups of oxygen compounds met with in organic chemistry.[4] It was an imposing edifice which he constructed under the general

idea of the analogy between liquid ammonia and water; and the classification of nitrogen compounds as belonging to the ammonia type in the same way as oxygen compounds may be considered to belong to the water type, was a stimulus and guide to investigation.

As will have been gathered from the preceding discussion, Franklin was essentially an experimentalist; and the fact that he worked in close association with only a comparatively small number of younger collaborators was due to his playing not only a directive but also a very active part in the experimental work of his research students. The scientific investigations in connection with which Franklin's name will always be remembered required great manipulative expertness, and the success of these researches was not only due in large measure to his own consummate experimental skill, but was a testimony to the careful training in experimental technique which he gave to his pupils. That his name appears at the head of only about half of the eighty-eight communications which came from his laboratory is an indication of his generous desire to detract in no way, through the prestige of his name, from the credit due to his younger collaborators.

Franklin's research work was strangely peculiar to himself and owed little or nothing to the influence of others; and the ideas on the basis of which his work was developed have given an extraordinary unity to his own investigations and a sure foundation to the work of others. He was a man whose memory we delight to honour.

# OBITUARY NOTICES.

## PRAMOD KRISOR BANERJEE.

### 1891—1937.

THE teaching of chemistry on modern lines in Bengal has sustained a great loss in the death of P. K. Banerjee, M.Sc., Professor of Chemistry in the Banknra College, Bengal.

Banerjee was born on November 16th, 1891, and came of a high-class family. He studied for his B.Sc. Honours and M.Sc. courses in the Presidency College, Calcutta, under the guidance of the doyen of Indian science, Sir Prafulla Chandra Râу. After serving as a Head Master for nearly fonr years, Banerjee joined the Bankura College in 1916 as Assistant Professor of Chemistry. He continued to serve in the same college as the Head of the Chemistry Department until, on October 16th, 1937, his promising career was terminated by a heart attack. Banerjee was an excellent teacher with a literary gift, and well acquainted with different Indian languages. He inspired the young men who came under his influence and many of his pupils have done well as chemists.

Notwithstanding his heavy teaching duties, Banerjee found time to carry on research work on oxidation processes and he published a paper (*Z. anorg. Chem.*, 1923, **128**, 343) on the oxidation of ferrous salt solutions under different conditions in air. His work in this line and on the preparation of natural dyes from Indian vegetables was not completed owing to ill-health. Banerjee, although shortsighted, was a keen sportsman. He was a straightforward, open-hearted man, and an excellent companion, always willing to help his students and friends at great personal sacrifice. He is survived by his aged parents, his wife, and seven children.

N. R. DHAR.

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## PERCIVAL WALTER CLUTTERBUCK.

### 1897—1938.

PERCIVAL WALTER CLUTTERBUCK was born at Leeds in 1897, and received his early education at the Leeds Central High School. He entered the Honours Chemistry School of the University of Leeds in 1914, being aided by a Board of Education grant. Two years later he joined the Royal Engineers (Gas Warfare Section) and saw active service in France. Having been gassed and rendered unfit for further service abroad, he was transferred to the Gas Warfare Research Section of the Royal Engineers and he remained in this until he was demobilised. For his military services he was awarded the O.B.E. Returning to Leeds in 1919, he completed his B.Sc. course, graduating with 1st Class Honours in 1922. In 1923 he was awarded the M.Sc. degree. He presented a thesis for the degree of Ph.D. in 1924 and in 1930 he received the degree of D.Sc.

In 1922 he commenced research work at Leeds under the late Professor J. B. Cohen. In the following year he went to Manchester, and for several years worked in collaboration with the writer. His first academic appointment was that of Demonstrator in Physiological Chemistry in the University of Manchester in 1924. After four years, having received a Beit Memorial Fellowship for Medical Research, he proceeded to the Lister Institute, where he studied fermentation problems with Sir Arthur Harden. A few months later, however, he was offered and accepted a post as Research Biochemist at Nobel's Explosives factory and went to work at Ardeer under the direction of Dr. H. Raistrick. Following the appointment of Dr. Raistrick to the Chair of Biochemistry at the London School of Tropical Medicine and Hygiene, Clutterbuck went to London to continue the work begun at Ardeer, and remained there until his untimely death on January 1st, 1938. In his first period at the School of Tropical Medicine he was still employed by Imperial Chemical Industries Ltd., but in 1933 he joined the academic staff of the School as Lecturer in Biochemistry. He became a Fellow of the Chemical Society in 1921, an Associate of the Institute of Chemistry in 1922 and a Fellow in 1928. From 1924 he served as Abstractor for the Biochemistry Section of Abstracts and his initials at the foot of Abstracts in this

Section must have become familiar to many Fellows of the Society, for he continued with this valuable work until his death. From 1931 onwards he was also an Abstractor for Nutrition Abstracts and Reviews.

Clutterbuck's first published work was on the preparation of the chloroamines of aryl and alkyl sulphonamides. Following this he began a study of the oxidation by hydrogen peroxide of normal fatty acids and, later, of acetoacetic acid. In the course of this work it was shown that in addition to the well-known β-oxidation of fatty acids, γ- and δ-oxidation also occurred. As a further product of oxidation of the γ- and δ-keto-fatty acids, succinic acid was isolated. This led him to examine the conditions under which succinic acid was formed in the body and its mode of conversion into malic acid through fumaric acid by the action of the enzymes succinodehydrogenase and fumarase. At Ardeer he began work on the biochemistry of moulds and bacteria, and throughout the succeeding years he continued almost entirely in this field. His first investigations were on the production of citric acid from sugar by moulds and of glucose from cellulose by certain bacteria. These were followed by a long series of investigations on the metabolic products of species of *Penicillium* and *Aspergillus*. They led to the isolation and characterisation of several new substances of great interest. Amongst these may be mentioned: the lactone of γ-hydroxy-βδ-dicarboxypentadecoic acid; chrysogenin, a pigment from *P. chrysogenum* Thom; mycophenolic acid; the closely related carolic, carolinic, carlic and carlosic acids—all from *P. Charlesii* G. Smith; geodin and erdin—two chlorine-containing products of *A. terreus* Thom—and terrein, also from the same organism. The separation of these substances, of which only small amounts are usually available, and the determination of their constitution demanded great skill. Its successful achievement is a testimony to Clutterbuck's powers as a chemist, and it is hardly necessary to emphasise its importance to the science of microbiology. Two years ago, with the clinical collaboration of Drs. Lucy Wills and Barbara Evans, Clutterbuck made an important discovery concerning the nature of the deficiency responsible for the nutritional anæmia of monkeys, which has its counterpart in human tropical anæmia. The hæmopoietic substance from liver, essential for the treatment of this condition, was shown to be different from that which is effective in pernicious anæmia.

Much of Clutterbuck's work was done in collaboration. His character and personal outlook made such co-operation easy, for although rightly proud of what he himself might contribute, he realised the absolute necessity of team work in the special field in which his activities lay. He was if anything over-modest, but this could not hide an enthusiasm for his work which was a delight to encounter. It is deplorable that his labours should be cut off when he had not even reached the height of his powers.

He was a very companionable man and made many friends. Their loss is a sad personal one and they will always hold him in grateful memory for what he achieved, for his simple honesty of purpose and for his gift of friendship.

In 1926 he married Muriel, the daughter of Mr. Barker North of Bradford. She and their two daughters survive him.

H. S. RAPER.

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## JOHN ALEXANDER DEY.

1868—1937.

DEY was born at Rothiemay in Banffshire and served his apprenticeship there as a pharmaceutical chemist with Messrs. Pirie & Sons. After a short period in Aberdeen he came to Edinburgh in 1887 and continued his studies at the Royal Dispensary School of Chemistry ("Duncan's") and qualified as a pharmaceutical chemist in 1890. In 1892 he joined the staff of Messrs. T. & H. Smith, the well-known manufacturing chemists, becoming Manager in 1899, and a Director in 1904.

He was actively concerned with the development of the firm's business and was responsible for the removal of the Works in 1906 to a much larger site on the outskirts of Edinburgh, the old name of the Blandfield Chemical Works being retained. Since then large additions to the Works have been carried out under his direction.

The War made great demands on the products of the firm, and Dey undoubtedly suffered in health from the strain of these years. He retired in 1935, much to the regret of his colleagues and staff.

Dey was elected a Fellow of the Society in 1925, and was also admitted a Fellow of the Royal Society of Edinburgh in the same year.

In his early days he was much interested in curling and he was also a keen fisherman.

He died in Edinburgh on December 18th, 1937, at the age of 69. His death removes a man of much administrative ability, and his loss is regretted by a large circle of friends.

ALEXANDER LAUDER.

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## SIR DAVID ORME MASSON.

### 1858—1937.

WITH the passing of Emeritus Professor Sir David Orme Masson on August 10th, 1937, Australia has lost one who for many years shared with the late Sir Edgeworth David the leadership of his adopted country in scientific effort and achievement. He was born in London on January 13th, 1858, his father, Professor David Masson, then occupying the chair of English Literature at University College. Seven years later his father accepted the Regius Chair of Rhetoric and English Literature in Edinburgh University and from 1893 until his death was Historiographer Royal for Scotland. Except for the early years in London, Masson received his training in Edinburgh, first at the Academy and later at the University, where he graduated in arts and science. Through his mother's family, the Ormes, whose home in Hampstead was a happy meeting ground of many leading figures of the time in literature and art, he made and retained numerous contacts with a life differing in many respects from that in which he later played so great a part on the other side of the world.

Physically strong and well built, a keen golfer and fond of swimming, tennis, and billiards, Masson played a considerable part in the life of his University both in his undergraduate days and later during his years as a research graduate. He was absent for a short time in 1880 when he studied under Wöhler at Göttingen, and shortly afterwards he joined Professor William Ramsay as his first assistant at Bristol, beginning a friendship which lasted until Sir William's death. Incidentally it is of interest to record that Masson was invited to succeed Ramsay when the latter retired from his chair at University College in 1913: but his roots in Australia were too deep by then to permit a return to Britain.

Ramsay was interested at the time in determinations of atomic volumes of elements at their boiling points and Masson joined him in the work on phosphorus (J., 1881, **39**, 50). Their results showed that it was necessary to ascribe two volumes to phosphorus, *viz.*, 20·8 in the free state and in compounds where it was quinquevalent and 25·3 where tervalent. Incidentally this led to $O{=}P{\equiv}Cl_3$ as the constitutional formula of the oxychloride instead of the previously accepted $Cl_2{=}P{-}O{-}Cl$: and it also indicated the untenability of the Schröder theory of "steres" as applied to boiling liquid compounds.

Returning to Edinburgh in 1881, Masson held a research scholarship under Professor Crum Brown for three years, carrying out work which gained him his D.Sc. degree in 1884.

During this time he took a leading part in founding the Students' Representative Council, the first of the kind in any University, and also the Students' Union. The existence of similar flourishing bodies in Melbourne to-day shows that his faith in such organisations was lasting.

The Edinburgh investigations included the preparation of glyceryl trinitrite and an examination of its properties (J., 1883, **43**, 348). This was followed by a study, in association with M. Hay, of the composition and properties of nitroglycerine, confirming its constitution as a trinitrate (*Proc. Roy. Soc. Edin.*, 1885, 87). With L. Dobbin he published in 1885 a study of the action of halogens on salts of trimethylsulphine, producing a number of compounds of the general formula $Me_3SX_3$, where X represents Cl, Br, or I, indiscriminately (J., 1885, **47**, 87). The question of the way in which the halogen atoms were linked together led to further work in the following year with tetramethylammonium

salts (J., 1886, **49**, 846), the result being the production of a continuous series of substances which appeared to show atomic-compound characters at one end and molecular-compound characters at the other; which, as the authors say, "appears to us to give some support to the position of those who deny the existence of two modes of combination, distinct in kind from each other." Two other papers in the same year (*ibid.*, pp. 233, 249) described work on sulphine salts containing the ethylene radical and discussed their constitutions.

In the eighties, the University of Melbourne, then some 30 years old, had decided that a single department of Natural Science, even under so omniscient a head as Sir Frederick McCoy, was no longer adequate for the times, and a division was made into the three Schools, Chemistry, Biology, and Physics. For a short time Kirkland was in charge of Chemistry, but in 1886 the chair fell vacant and the choice of a successor lay between Masson and W. H. Perkin, jun. The decision to take the former determined the main line of future development of the new school, since from this time Masson turned steadily towards physico-chemical work rather than organic. Not very long afterwards, Baldwin Spencer was invited to take the chair of Biology and then Thomas Ranken Lyle followed in that of Physics. It is rarely that a Colonial University has been as fortunate as was Melbourne in securing so remarkable a trio of young men for its science schools. Each of them made an international reputation for himself and all three were honoured with knighthood. Between them they created and developed high standards in teaching and research.

At first the number of students in the Chemistry School was small: but growth was steady and soon became rapid. In later years the first-year classes alone sometimes rose to 250. As a lecturer, Masson has become almost a tradition for his clarity of thought, logical array of facts, perfect diction and, combined with these, remarkable facility in bench experiments and demonstrations. He laboured under difficulties only appreciated by those who have worked in distant parts of the Empire. Teaching duties were very heavy; the supporting staff was inadequate in number, and funds for apparatus and chemicals were scanty. Often enough the line of investigation followed was determined by its relative cost.

There was little opportunity in the early years in Melbourne for laboratory work, though with J. B. Kirkland, the son of his predecessor, Masson continued his work on reactions of halogens on salts of tetraethylphosphonium and on the preparation of salts of triethylsulphiue, tetraethylphosphonium and analogous bases (J., 1889, **55**, 126, 135). Two years later, with one of his earliest students, N. T. M. Wilsmore, he published a paper entitled "Does magnesium form compounds with hydrocarbon radicles?" (Proc., 1891, 16). This describes unsuccessful experiments aiming at the production of magnesium ethide and methide by interaction of magnesium and ethyl iodide. There is no doubt that these workers came very close to, but just missed, the formation of Grignard's reagent which later played an important rôle in organic synthesis.

At this time Masson returned to his earlier work on molecular volumes and published a discussion of the relation in liquids between these, the boiling points and chemical characters (*Phil. Mag.*, 1891, **30**, 412). The law was formulated that for liquids of the same type (such as alkyl halides) the volumes of unit mass are inversely proportional to the molecular weights and directly proportional to the absolute temperatures when compared at temperatures at which the vapour pressures are equal; thus $V_T/T$ is constant, where $T$ is the absolute temperature of boiling and $V_T$ the molecular volume at it. From this it may be deduced that the molecular heat of vaporisation is directly proportional to the absolute boiling point; a useful generalisation, the applicability of which, however, is limited.

In these years Masson became deeply interested in the development of the theory of solutions as propounded by van 't Hoff, Arrhenius, Ostwald and their school. In his presidential address to Section B of the Australasian Association for the Advancement of Science in 1891, published in part in *Nature* (**43**, 345), he drew attention to the essential similarity of the processes of solution and evaporation, pointing out that in the case of a system of solid and solvent, the solid would have a solution melting point lower than its true melting point. Above this temperature two liquid phases, each a saturated solution,

would occur. With rise of temperature these two liquids would become homogeneous at a temperature depending on the original composition. To the highest attainable temperature, at which both layers became identical, and above which each component is infinitely soluble in the other, he gave the name "critical solution temperature", which has been retained ever since.

Very little came from his laboratory for the next few years, but in 1896 he published a note in the *Chemical News* (**72**, 283) discussing the question of whether hydrogen should be placed at the head of Group I or at the head of Group VII in the Periodic Classification. There was no hesitation in placing it in the latter position. It was in the previous year that Masson had produced his modification of Mendeléef's periodic classification of the elements using the now familiar folder with a flap on which all sub-group elements appeared. When Ramsay discovered helium, Masson immediately placed it with argon in a new Group VIII, leaving room for the other undiscovered elements of zero valency. It is curious that this very satisfactory folder arrangement, though adopted in his class rooms at University College by Ramsay, was not more generally used. It broke down, of course, with the rare-earth metals, but otherwise was very similar to Bohr's grouping of later times.

From now on Masson's laboratory work dealt mainly with ionisation in aqueous solutions and with problems in chemical dynamics. With B. D. Steele, then a student, he investigated the blue salt of Fehling's solution and other cuprotartrates (J., 1899, **75**, 725) as a side study associated with his development of a new method for the direct comparison of ionic velocities. They readily proved that the kations were colourless and that the copper was present in the anions: and from that proceeded to the preparation of a number of other cuprotartrates of varying solubility and stability.

His work on the velocity of migration of ions is perhaps that for which Masson was best known: in fact the use of his simple experimental apparatus came to be very general as a laboratory exercise (*Phil. Trans.*, 1899, *A*, **192**, 33). Besides a battery, resistance, voltmeter, *etc.*, it consisted of two flasks with side necks into which fitted tightly the ends of a straight, horizontal, narrow glass tube about 12 cm. long. Glass-blowing was not a well-developed art in Melbourne in those days and the glass-bottle works which undertook the production of the double-necked flasks would not consider an output of fewer than a gross. For years afterwards there was never a shortage of this particular item in the students' store-room!

It having been shown that only a slight reduction in mobility of ions was brought about in a 12% gelatin "gel" as compared with a free solution, Masson used this to give stability to the solutions examined, which to begin with were of alkali chlorides. Platinum electrodes were placed in the flasks, which contained salts with coloured kation (*e.g.*, $Cu^{\cdot\cdot}$) and anion (such as $CrO_4''$) respectively, each being less mobile under like conditions than the positive and negative ions of the solute in the jelly. With an application of about 40 volts the experiment proceeds readily, with sharp boundaries between the coloured and the colourless portions at either end. In his analysis of the results Masson showed that the progress of the coloured ions is determined by the velocity of the colourless ions which they follow. The relative rates of movement of the boundaries give the ratio of the mobilities of the colourless ions which are at any moment under equal potential slope, and not of the coloured ions themselves which are not under like gradient; and hence are obtained the transport numbers for the solute in the tube. For salts of sodium, potassium and ammonium, the anionic migration numbers were rather lower than those found by Hittorf's method: the relative velocities directly measured agreed well with those deduced from Kohlrausch's conductivity figures.

Later this method was carried further by Steele, who showed that it was possible by simple devices to do without the gelatin and the coloured ions thus greatly extending the range of applicability of the direct measurement.

About the same time Masson and his colleague in the physiology department, C. J. Martin, made some measurements of conductivity, of considerable accuracy for those days, to determine the effect of varying viscosity on conductivity. The alteration of viscosity was brought about by addition of sucrose in increasing amount; and incidentally

proof was obtained of a reaction between caustic alkalis and the sugar. This work was later carried much further by W. Heber Green.

A useful laboratory note on Iceland spar as a standard in volumetric analysis was published in 1900 (*Chem. News*, 1900, **81**, 73). The method is now standard laboratory practice and is thoroughly satisfactory provided that no opportunity is given for the formation of calcium bicarbonate during the reaction with hydrochloric acid. Shortly afterwards, Masson began an investigation into the hygroscopic character of cellulose, in which he sought exact information as to the absorption of moisture by cellulose and the laws governing it. This was expanded later in association with one of his senior students, E. S. Richards (*Proc. Roy. Soc.*, 1906, **78**, 412), their paper being published just a little later than one on similar lines by Trouton and Pool.

A dynamical study in 1907 (J., 1907, **91**, 1449) of the highly exothermic action of hydrogen peroxide on potassium cyanide in aqueous solution was prompted by some observations made earlier by C. J. Martin which seemed irreconcilable with any simple theory of oxidation. From analyses of the finished products and by titration of residual cyanide and peroxide during the course of the action, it was shown that the products of oxidation are potassium cyanate and potassium and ammonium carbonates. Cyanate is first formed and is then hydrolysed to carbonate through the catalytic agency of the peroxide. At the same time a part of the cyanide is converted by hydrolysis, but without oxidation, into formate and ammonia, and here too the peroxide acts as catalyst. About four-fifths of the original cyanide is converted by oxidation into cyanate and carbonate while the remaining one-fifth is hydrolysed to formate. Alkali retards the action and so does acid : only with sufficient sulphuric acid to convert all the cyanide into hydrogen cyanide is oxamide (formerly assumed to be the main product) formed. A note with A. C. Cumming (*Chem. News*, 1906, **93**, 5, 17) dealt with incidental problems in the volumetric estimation of cyanates and carbonates.

This work with cyanates led Masson to a fuller study of the decomposition of metallic cyanates by water (*Z. physikal. Chem.*, 1910, **70**, 290) in association with his son Irvine, now professor of Chemistry at Durham. With cyanates of metals which form insoluble carbonates there are two consecutive reactions, the first being a slow hydrolysis of cyanate to carbonate, which is precipitated, and to ammonium ions, and the second a relatively rapid reaction between ammonium and cyanate ions to form carbamide. The cyanates of sodium and potassium decomposed to give the corresponding carbonates, ammonium carbonate and carbamide. Any reverse change of the carbamide is inappreciable. The products, especially ammonium carbonate, accelerate the reaction.

In the same year he completed with Miss Green a study of the dynamics of the decomposition of persulphuric acid and its salts in aqueous solution. They confirmed the accepted view that potassium and sodium persulphates decompose unimolecularly and that acids accelerate the action. As acid sulphate is produced, it was necessary to explain why the action was not autocatalytic rather than simple unimolecular. This they did by formulating the change by the ionic equation :

$$S_2O_8' + H_2O = 2HSO_4' + \tfrac{1}{2}O_2$$

there being practically no hydrogen ions produced, since under the conditions of the experiments sulphuric acid could be regarded as monobasic. The courses of the action differed markedly in the three cases of (i) neutral sodium, potassium and ammonium persulphates, convertible into acid sulphates, (ii) persulphuric acid itself, which doubles its acidity by conversion into sulphuric acid, and (iii) barium persulphate, which produces persulphuric acid and barium sulphate. The influence of various additional solutes was carefully examined.

From this time onwards Masson became steadily more absorbed in administrative work within and without the University with the result that his opportunities for personal laboratory work were greatly lessened. He took a keen interest always in the development of ideas on the constitution of atoms and in a paper in 1921 (*Phil. Mag.*, 1921, **41**, 281) he pointed out that if $N$ is the atomic number, and p and e represent proton and electron respectively, all nuclei from He to U can be expressed by the formula $(p_2e)_N(pe)_n$.

where $n$ has any appropriate value from 0 to 54. To include hydrogen $n$ must equal $-1$. Emission of $\alpha$- and $\beta$-particles can be represented by simple equations. A chart of radio-active transmutations for the radium, actinium, and thorium series was constructed in which isobares were along horizontal isotopes on vertical, and isoclines (with the same $n$) on diagonal lines. This made an interesting supplement to the Periodic Classification Chart of 1895.

After his retirement from active teaching at the end of 1923, Masson's interest in the progress of chemical theory continued unabated. In particular he attacked the problem presented by strong electrolytes at all concentrations, being dissatisfied with the current view of complete dissociation. The results of this work were given to the Sydney meeting of the Australian and New Zealand Association for the Advancement of Science in a note-worthy paper, which was his last. The basis of this study of conductivity–concentration relations was a recognition of the fact that neither Arrhenius's assumption of constant ionic mobility with variation of degree of ionic dissociation, nor Debye and Hückel's assumption of constant (total) dissociation with varying mobility, leads to conclusions sufficiently in accordance with facts in other than very dilute solutions. The discussion led to a purely empirical equation which covered the best available experimental conduct-ivities up to high concentrations and permitted certain interesting speculation as to its precise theoretical significance.

When Masson arrived in Melbourne its population was under 400,000: in 1937 it reached 1,025,000. In such a rapidly growing community there were many public activities demanding the best effort that men of his type could offer, and throughout his life he was intimately identified with many civic and national movements of the times. In public and social work he was ever admirably supported by Lady Masson, C.B.E., a daughter of the late Professor Sir John Struthers, of Aberdeen and Edinburgh.

Shortly after his arrival in Melbourne, Masson was appointed to membership of the Victorian Board of Public Health, which was superseded by a new organisation in 1890. In that year he acted on a royal commission charged with an examination of the problem presented by the sanitation needs of Melbourne, a problem very satisfactorily dealt with in the succeeding years. He was chairman of a board appointed in the early days of Federation by the Commonwealth Government to report on silver coinage.

The organisation of Antarctic exploration was always one of his keen interests. He was a very active member of the committee which organised Mawson's first expedition in 1911—14: he was also on the committee appointed by the Commonwealth Government to organise the expedition for the relief of Sir E. Shackleton's Antarctic (Ross Sea) party. In 1911—13 he was President of the Australasian Association for the Advancement of Science and was the leader in the project for bringing the British Association to Australia in 1914, and chairman of the organising committee.

These were busy years, for from 1912 to 1916 he was president of the professorial board of the University and a member of its Council. During the war he served on certain special committees dealing with munitions and naval matters: but possibly his chief work of that time commenced in 1915 when the then Prime Minister, Mr. W. M. Hughes, invited him to act as chairman of a committee to draft a scheme for a Commonwealth Institute of Science and Industry. Political support failed at the crucial time, but the determination of Masson was chiefly responsible for the initiation of much valuable national research and, in 1920, for the establishment of an institute. In 1926 this was reorganised and became the present Council for Scientific and Industrial Research, on which Masson was an invaluable member until his death.

As founder of the Melbourne University Chemical Society, the Society of Chemical Industry of Victoria and, with others, of the Australian Chemical Institute and its first President (1917—20), Masson has left behind him very flourishing institutions in which his name is held in reverent esteem. With Sir Edgeworth David he was mainly responsible for founding the Australian National Research Council in 1921 and was its president in 1922—23. In the latter year he was also president of the second Pan-Pacific Science Congress held in Melbourne and Sydney. He was elected to the Royal Society in 1903; created C.B.E. in 1918 and K.B.E. in 1923. His old University of Edinburgh conferred

an LL.D. degree upon him in 1924, *honoris causa.* A Masson Lectureship was established in his honour by the Australian National Research Council a few years ago.

It is given to few men to combine such academic brilliance and personal charm as distinguished Sir David Masson, with so marked a capacity for practical achievement in the development of national life in a young British community. He was a great Empire builder, inspired by, and inspiring, the highest ideals of service. He will ever be remembered with pride and deep affection by students and colleagues and by a very wide circle of friends.

A. C. D. RIVETT.

## JOHN JAMES MORGAN.

### 1865—1937.

JOHN J. MORGAN, whose death took place on October 30th, 1937, was born at Tredegar in 1865 and was educated at Abergavenny Grammar School. On leaving school he became a pupil under Mr. A. E. Tncker, and was appointed later as Head Assistant Analyst to the Rhymney Iron and Steel Co. After three years, he joined the Ebbw Vale Iron, Steel and Coal Co. as Chemist, subsequently becoming head Assistant Analyst to the Blaenavon Iron, Steel and Coal Co., and later Chief Chemist to Messrs. Cammell, Laird and Co., Ltd., at Workington. Subsequently he went into practice as a Consulting Analyst, Assayer and Sampler in Manchester.

At the time of the Russian Revolution in 1917 Morgan was in the Caucasus district, examining ore mines; on his return, he worked with the Admiralty until the end of the war, and then resnmed his private practice until his retirement owing to ill-health. He had a wide and detailed knowledge of his work, and specialised particularly in ores. He was the author of "Aids to Analysis and Assay of Ores, Metals, Fuels, etc.," "Blast Furnace Practice," "Notes on Foundry Practice," and of other books on various branches of his work. He also contributed to various technical journals.

Morgan was elected a Fellow in 1888.

## CHARLES WATSON.

### 1861—1937.

CHARLES WATSON died very suddenly on September 9th, 1937. He was one of the oldest Fellows of the Society, having been a Fellow for 52 years.

He was born on March 10th, 1861, at Hamilton, Ontario, and came to Stockton-on-Tees at the age of five. He was educated at the King James I Grammar School at Bishop Auckland. His training as an analytical chemist was received in the laboratory of Messrs. Sadler and Co.'s works at Middlesbrough. Afterwards, in conjunction with the late Mr. H. Peile, he carried on a chemical works at Walsden, near Todmorden, for the manufacture of soap, sheep dip, etc. Subsequently he obtained an appointment in Buenos Aires and after a short period there he returned in 1903 to become Works Manager of the Dawsholm Tar and Ammonia works, Glasgow. He left Glasgow in 1906 for Birmingham, where he was Works Manager at Messrs. Josiah Hardman and Co. until 1909. He then retired from active chemical work, but continued to live at Moseley, Birmingham, for a number of years and later came to Devonshire to reside, first at Ottery St. Mary and in 1935 at Exeter.

He was twice married. His first wife, whom he married in 1906, was a daughter of Alderman E. Henderson of Stockton-on-Tees. She died in 1929 at Ottery St. Mary. In 1934 he married Mrs. Edith Fawdye.

Watson was a man of quiet and genial disposition and, as one of his former assistants describes him, "a thorough gentleman who was esteemed and appreciated by every employee with whom he had to deal."

Although he retained an interest in chemistry up to the end (he was often present at public lectures on chemical subjects given at University College, Exeter), he had many

other interests, particularly those of the mechanical type. During the War he put one of these interests into practical form in manufacturing tools required by munition workers. During his stay in Devonshire he interested himself in bee-keeping and in metal and woodwork, and among other things constructed several electric clocks. H. T. S. BRITTON.

## ALFRED EDWARD WILLIAMSON.

1878—1937.

ALFRED EDWARD WILLIAMSON, who died on October 7th, 1937, was born in Liverpool on November 6th, 1878. Leaving school at an early age, he entered the drug trade with Messrs. Evans, Sons, and Co. (now Evans, Sons, Lescher, and Webb, Ltd.) at Liverpool.

In 1900 he qualified as an accountant; later he became manager of Messrs. Clay, Dodd, and Co., Liverpool, and in 1911 joined Messrs. John Thompson, Ltd., Wholesale Chemists, Liverpool.

In 1921 Williamson became a director of Messrs. John Thompson (Wholesale Druggists, 1921), Ltd., and in 1929 he was appointed Joint Managing Director and Secretary, which position he held until his death.

He was elected a Fellow of the Chemical Society in 1931. H. HUMPHREYS JONES.

## ANDREW YOUNG.

1873—1937.

ANDREW YOUNG, whose death took place at Cape Town on November 7th, 1937, was born in Perth, Scotland, in 1873. He was educated at Perth and at Edinburgh University, where, as a pupil of Professor James Geikie and Sir John Flett, he obtained honours in Geology.

After undergoing a course of training at the Church of Scotland Training College for Teachers, Young occupied several educational posts, including those of Organiser of Technical Education in Gloucestershire, and Lecturer in Geology at the Heriot Watt College, Edinburgh.

In 1902, at the age of 29, he was appointed to the Chair of Geology at the South African College, Cape Town, and continued to hold this Chair when the College was incorporated as the University of Cape Town in 1918 until the time of his death. He took an active part in the administrative and other activities of the University.

Among the well-known men who studied geology under his tuition were the late Dr. Percy Wagner, whose books on diamond and platinum occurrences in South Africa are standard works, and Dr. J. W. Gevers, Professor of Geology at the University of the Witwatersrand.

The study of underground water conditions in South Africa absorbed much of Young's attention. In recognition of his discovery and investigation of tidal phenomena in the subterranean waters of the Karroo, the University of Edinburgh conferred on him the degree of D.Sc.

Young travelled extensively in the prosecution of his work, visiting among other countries Algeria and Namaqualand to examine the geology of these countries. He also made a close study of petroleum throughout the world and was considered an authority on the subject.

A man of wide intellectual interests, Young also had an extensive and detailed knowledge of a great variety of other subjects. His hobby was the collection of Eastern carpets and rugs. He was an expert on this subject and his own collection is a very fine one.

Young was elected a Fellow of the Chemical Society in 1903.

# *Synthesis of Polyenes.*

THE SIXTH PEDLER LECTURE, DELIVERED BEFORE THE CHEMICAL SOCIETY ON JANUARY 27TH, 1938.

By RICHARD KUHN.

IT is with great pleasure that I most sincerely thank the Chemical Society for the invitation, with which they have honoured me, to give the sixth lecture in memory of Sir Alexander Pedler. With admiration I have become acquainted with the career of this natural philosopher, whose investigations ranged from Organic Chemistry through Physics to Astronomy. In contrast to this versatility stands the problem with which I, aided by a number of outstanding collaborators, have been engaged for more than ten years. This lies in the artificial preparation of compounds containing the largest possible number of conjugated double bonds. I propose to speak to-night of some of the results obtained so far in this scheme of research. The synthetic methods which have proved most serviceable will be given most prominence. I can only refer briefly in a few places to the connection between chemical constitution and physical properties. In this connection, there are, besides the regularities in melting points (Kuhn and Grundmann, *Ber.*, 1936, **69**, 224), the exhaustive measurements of the absorption and fluorescence spectra carried out by my prematurely deceased colleague, K. W. Hausser (Hausser, Kuhn, Smakula, and Kreuchen, *Z. physikal. Chem.*, 1935, *B*, **29**, 363; Hausser, Kuhn, Smakula, and Hoffer, *ibid.*, p. 371; Hausser, Kuhn, Smakula, and Deutsch, *ibid.*, pp. 378, 384; Hausser, Kuhn, and Seitz, *ibid.*, p. 391; Hausser, R. Kuhn, and E. Kuhn, *ibid.*, p. 417; Hausser and Smakula, *Angew. Chem.*, 1935, **47**, 657; **48**, 152).

## A. $C_6H_5{\cdot}[CH{:}CH]_n{\cdot}C_6H_5$ ($n = 1, 2, 3, 4, 5, 6, 7, 8, 11, 15$).

For the synthesis of the diphenyl polyenes (Kuhn and Winterstein, *Helv. Chim. Acta*, 1928, **11**, 87), we have to-day the following methods:

1 : 6-Diphenylhexatriene (III) (Smedley, J., 1908, **93**, 372) is best obtained by treating a suspension of hydrocinnamoin in ether with the calculated quantity of phosphorus di-iodide ($P_2I_4$). The di-iodide, most probably formed as intermediate, spontaneously splits off iodine, and one obtains in a few minutes the yellow hydrocarbon in theoretical yield:

$$\text{(I)}\ \mathrm{Ph{\cdot}CH{:}CH{\cdot}CHO + 2H + OHC{\cdot}CH{:}CHPh}$$
$$\downarrow \mathrm{Zn}$$
$$\text{(II)}\ \mathrm{Ph{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}CH(OH){\cdot}CH{:}CHPh}$$
$$\downarrow \mathrm{P_2I_4}$$
$$\text{(III)}\ \mathrm{Ph{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CHPh}$$

This reaction, discovered with Winterstein (*loc. cit.*) in 1927, can be carried out not only with 1 : 2-glycols, but also, as Kuhn and Wallenfels (unpublished work) have recently shown, with 1 : 4-glycols and with 1 : 6-glycols, and thus has general application in the synthesis of the polyenes. The 1 : 4-glycols (VI) are readily obtainable by condensation of polyene aldehydes with acetylenedimagnesium bromide (IV), and subsequent partial hydrogenation of the acetylenic glycols (V). Diphenyloctatetraene was obtained in very good yield by this method as follows:

$$\mathrm{Ph{\cdot}CH{:}CH{\cdot}CHO + (IV)Br{\cdot}Mg{\cdot}C{:}C{\cdot}MgBr + OHC{\cdot}CH{:}CHPh}$$
$$\downarrow$$
$$\text{(V)}\ \mathrm{Ph{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}C{:}C{\cdot}CH(OH){\cdot}CH{:}CHPh}$$
$$\downarrow \mathrm{H_2}$$
$$\text{(VI)}\ \mathrm{Ph{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}CH{:}CH{\cdot}CH(OH){\cdot}CH{:}CHPh}$$
$$\downarrow \mathrm{P_2I_4}$$
$$\text{(VII)}\ \mathrm{Ph{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CHPh}$$

The *phosphorus di-iodide method* permits therefore of the preparation not only of compounds with an odd, but also of those with an even, number of conjugated double bonds.

The 1 : 6-glycols are obtained according to Straus and Kollek (*Ber.*, 1926, **59**, 1664) in a similar way, diacetylenedimagnesium bromide, Br·Mg·C:C·C:C·MgBr, being used.

Kuhn and Winterstein (*loc. cit.*) first obtained 1 : 12-diphenyldodecahexaene (IX) by condensation of 5-phenylpentadienal (VIII) with succinic acid in the presence of lead oxide, a mixture of glacial acetic acid and acetic anhydride being used as solvent :

$$\text{(VIII) Ph·CH:CH·CH:CH·CHO} + \text{HO}_2\text{C·CH}_2\text{·CH}_2\text{·CO}_2\text{H} + \text{OHC·CH:CH·CH:CHPh}$$

$$\downarrow$$

$$\text{(IX) Ph·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH:CHPh}$$

They obtained the yellow 1 : 8-diphenyloctatetraene by using cinnamaldehyde in place of phenylpentadienal, and the copper-coloured 1 : 16-diphenylhexadecaoctaene from 7-phenylheptatrienal. In general, with succinic acid as the " middle piece," this *lead oxide method* yields hydrocarbons with an *even* number of conjugated double bonds.

The synthesis of diphenyl polyenes with an odd number of double bonds ($n = 5, n = 7$), was achieved by substitution of dihydromuconic acid, $HO_2C·CH_2·CH{:}CH·CH_2·CO_2H$, for succinic acid.

It would be expected that dihydrohexatriene-1 : 6-dicarboxylic acid, $HO_2C·CH_2·CH{:}CH·CH{:}CH·CH_2·CO_2H$, should give rise to even-number hydrocarbons by the lead oxide method. The recent synthesis of this substance has made it possible to attempt this experiment. Kuhn and Grundmann (*Ber.*, 1936, **69**, 1757) found that butadiene-1 : 4-diacetic acid (X), prepared by them, did indeed yield 1 : 12-diphenyldodecahexaene (IX) by condensation with cinnamaldehyde and lead oxide :

$$\text{Ph·CH:CH·CHO} + \text{(X)HO}_2\text{C·CH}_2\text{·CH:CH·CH:CH·CH}_2\text{·CO}_2\text{H} + \text{OHC·CH:CHPh} \longrightarrow \text{(IX)}$$

Another synthesis of the same hydrocarbon was rendered possible, when a year ago Kuhn and Wallenfels (*Ber.*, 1937, **70**, 1331), succeeded in preparing the orange-coloured 11-phenylundecapentaenal $Ph·[CH{:}CH]_5·CHO$, and the deep red 15-phenylpentadecaheptaenal, $Ph·[CH{:}CH]_7·CHO$, by condensation of cinnamaldehyde with crotonaldehyde in the presence of piperidine acetate. By the action of benzylmagnesium chloride on the pentaenal (XI) they obtained by the usual *Grignard reaction* the alcohol (XII), which was not isolated. This was converted into 1 : 12-diphenyldodecahexaene (IX) by removal of water and formation of the conjugated double bond system :

$$\text{(XI) Ph·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CHO} + \text{ClMg·CH}_2\text{Ph}$$
$$\text{(XII) Ph·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH(OH)·CH}_2\text{Ph}$$

The hexaenes prepared by these *three* different methods were shown to be identical by mixed melting point (267°) and by the positions of their very sharp absorption bands.

We had endeavoured for some time to extend the series of diphenyl polyenes still further. But it turned out that the well-proved lead oxide method began to fail at about eight conjugated double bonds. We recognised that any considerable progress would only be made possible by the discovery of a fundamentally new synthetic method. Such a method was recently found with K. Wallenfels (Kuhn, *Angew. Chem.*, 1937, **50**, 703). The oxygen atom of the polyene aldehydes, just like that of the simple aldehydes, can be replaced by an atom of sulphur by the action of hydrogen sulphide under suitable conditions. Similarly, the preparation of selenoaldehydes by the action of hydrogen selenide is also possible. It was known that sulphur may be split off from thiobenzaldehyde, and that the hypothetical bivalent radical benzylidene so formed dimerises to stilbene. This reaction can now also be carried out with polyene thio- and seleno-aldehydes. The removal of the sulphur is best brought about by metals such as copper, metal carbonates, various reducing agents, and also by certain amines such as piperidine

From 11-phenylundecapentaenal (XI), we obtained in this way 1 : 22-diphenyldocosaundecaene (XIV) :

(XI) Ph·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CHO

↓ $H_2S$, $H_2Se$

(XIIIa) Ph·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CHS
(XIIIb) Ph·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CHSe

↓ Cu

(XIV) Ph·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH
‖
Ph·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH

This hydrocarbon was violet-black, and had a marked metallic lustre. It melted at 318°. From 15-phenylpentadecaheptaenal (XV) we succeeded in preparing 1 : 30-diphenyltriacontapentadecaene (XVII) by means of the corresponding thioaldehyde (XVI) :

(XV) Ph·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CHO

↓

(XVI) Ph·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CHS

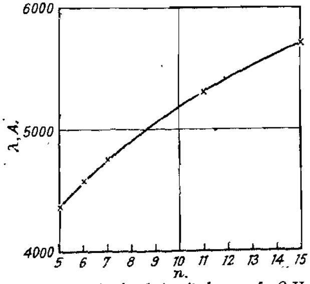
↓

(XVII) Ph·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH
‖
Ph·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH:CH·CH

This hydrocarbon with thirty methene groups in a straight chain is the highest member of the polyene series known at present. The solid is greenish-black, and its solutions are violet-red. The constitution given follows from the position of the absorption bands. These, together with those of the lower homologues, fit into a regular series, as was shown with Hausser :

| | |
|---|---|
| $n = 5$ | $\lambda = 4340$ A. in nitrobenzene |
| $n = 6$ | $\lambda = 4580$ A. in nitrobenzene |
| $n = 7$ | $\lambda = 4740$ A. in nitrobenzene |
| $n = 11$ | $\lambda = 5300, 4930, 4620$ A. in nitrobenzene |
| $n = 15$ | $\lambda = 5700, 5320$ A. in nitrobenzene |

FIG. 1.




*Wave-lengths of the first absorption bands in nitrobenzene for* $C_6H_5\cdot[CH:CH]_n\cdot C_6H_5$.
n = *number of conjugated double bonds.*

We have not yet succeeded in preparing the pentadecaene in the pure state. The ability to sublime in a high vacuum falls off much lower down the series, and the solubility decreases so rapidly with the increasing number of conjugated double bonds that we were unable to find a solvent from which to recrystallise the pentadecaene.

B. $CH_3\cdot[CH{:}CH]_n\cdot CHO$ ($n$ = 1, 2, 3, 4, 5, —, 7, —, 9) *and* $CH_3\cdot[CH{:}CH]_n\cdot CO_2H$ ($n$ = 1, 2, 3, 4, 5, 6, —, 8).

The fundamental method for the synthesis of the purely aliphatic polyenes, to which we now turn, is the aldol-like condensation of acetaldehyde with itself. A convenient preparation of sorbaldehyde was discovered (Kuhn and Hoffer, *Ber.*, 1930, **63**, 2164; 1931, **64**, 1977) in 1930 in the action of piperidine on a mixture of acetaldehyde and crotonaldehyde. The attempt to condense crotonaldehyde with itself under the same conditions was, however, unsuccessful. As was found later (Kuhn, Badstübner, and Grundmann, *Ber.*, 1936, **69**, 98) the crotonaldehyde condensed in the required sense only after exposure to sunlight, or after irradiation with a mercury lamp. This effect was apparently due to the formation of a small quantity of crotonic acid by autoxidation. If the irradiated " active " crotonaldehyde was shaken with alkali, it became " inactive " again. If some crotonic acid was added, the condensation proceeded at once even in the dark. We also found that the crotonic acid could be replaced by other acids. The sole necessary condition is that the amine used as catalyst should be present as a salt, and not as the free base. For preparative work " piperidine acetate," an equimolecular mixture of piperidine and glacial acetic acid, is employed. Since then we have used this catalyst frequently for aldehyde condensations, and Kuhn and Grundmann (*Ber.*, 1937, **70**, 1318) have obtained with it a series of higher vinylene homologues of crotonaldehyde (XVIII) :

(XVIII) $CH_3\cdot CH{:}CH\cdot CHO$  (XIX) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CHO$

(XX) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CHO$  (XXI) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CHO$

(XXII) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CHO$

(XXIII) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CHO$

(XXIV) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CHO$

100 G. of the orange-red dodecapentaenal ($n$ = 5) can be obtained by the action of piperidine acetate on 1 kg. of crotonaldehyde. The hexadecaheptaenal ($n$ = 7) forms deep red needles of melting point 218° (Kuhn, Grundmann, and Trischmann, *Z. physiol. Chem.*, 1937, **248**, IV). Bernhauer (*Biochem. Z.*, 1932, **249**, 199; **251**, 173) showed that the yield of octatrienal from the condensation of crotonaldehyde varied widely with the kind of piperidine used. This is also true of the higher polyene aldehydes. In recent experiments (Kuhn and Grundmann, unpublished work) the catalyst and the reaction conditions have been so much improved that 40% of the cheap crotonaldehyde is converted into a deep red, crystalline mixture of polyene aldehydes.

All these aldehydes condense with malonic acid in pyridine to give the carboxylic acid with one double bond more. In the case of the higher aldehydes, it is essential to use piperidine as catalyst in the Doebner reaction; with the lower aldehydes, addition of piperidine considerably lowers the yields, since here the condensation of the aldehyde with itself becomes too rapid. On the other hand, the higher aldehydes condense but slowly with themselves in the presence of piperidine salts, so that the reaction with the methylene group of the malonic acid predominates (Kuhn and Grundmann, *Ber.*, 1937, **70**, 1318).

A further difference between the " lower " and the " higher " polyene aldehydes lies in the fact that the former with malonic acid and piperidine yield the monocarboxylic acids directly, whereas the higher aldehydes in the presence of piperidine yield only the dicarboxylic acids. These must then be converted into the corresponding polyene carboxylic acids by decarboxylation. This is carried out by boiling with acetic acid and acetic anhydride rather than by dry thermal decomposition (*idem, loc. cit.*).

(XXV) $CH_3\cdot CH{:}CH\cdot CO_2H$  (XXVI) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CO_2H$

(XXVII) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CO_2H$

(XXVIII) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CO_2H$

(XXIX) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CO_2H$

(XXX) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CO_2H$

(XXXI) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}C(CO_2H)_2$

The first coloured compound of this series is the decatetraenecarboxylic acid ($n$ = 4) (Kuhn and Hoffer, *Ber.*, 1930, **63**, 2164; 1931, **64**, 1977). The hexadecaheptaenalmalonic

acid ($n = 8$) (Kuhn, Grundmann, and Trischmann, *Z. physiol. Chem.*, 1937, **248**, IV) crystallises from pyridine in deep violet needles. Eight molecules of hydrogen are taken up during the catalytic hydrogenation. Subsequent distillation yields a colourless oil, which solidifies at once. This crystallises from alcohol in greasy shining platelets of melting point 69°, which are identical in all their properties with natural stearic acid.

The above total direct synthesis of stearic acid is also of interest in connection with the biological synthesis of fatty acids in Nature. This may be founded on a catalytic condensation of eight molecules of acetaldehyde in a straight chain. We are not as yet acquainted with the intermediate stages actually occurring in Nature, but evidently not only acetaldehyde, but also its derivatives or predecessors like pyruvic acid (Smedley-Maclean), may undergo the aldol condensation. During metabolism, reduction certainly occurs at an earlier stage than in our synthesis, since highly unsaturated fatty acids, which could be detected by their colour, have not as yet been observed in either plants or animals. The catalytic hydrogenation of polyene aldehydes proceeded smoothly in all cases, yielding the corresponding saturated alcohols. In this way pure cetyl alcohol of melting point 48·5° was obtained from hexadecaheptaenal ($n = 7$) (Kuhn, *Angew. Chem.*, 1937, **50**, 703).

## C. $CH_3\cdot[CH{:}CH]_n\cdot CH_3$ ($n = 1, 2, 3, 4, —, 6$).

The polyene aldehydes react normally with alkylmagnesium halides, forming the corresponding carbinols. Kuhn and Grundmann (*Ber.*, 1938, **71**, 442), who established this, also found an excellent means for dehydrating the secondary alcohols so obtained, and thus preparing the aliphatic polyene hydrocarbons. This reagent is a 1—2% solution of *p*-toluenesulphonic acid in ether.

We obtained from sorbaldehyde (XXXII) and ethylmagnesium bromide 1 : 6-dimethylhexatriene (XXXIV), previously prepared by other methods (Urion, *Ann. Chim.*, 1934, [ii], **1**, 5).

(XXXII) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CHO + BrMg\cdot CH_2\cdot CH_3$

↓

(XXXIII) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH(OH)\cdot CH_2\cdot CH_3$

↓

(XXXIV) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH_3$, m. p. 52°

We also obtained the new compounds 1 : 8-dimethyloctatetraene (XXXVI) from octatrienal, and 1 : 12-dimethyldodecahexaene (XXXVIII) from dodecapentaenal:

(XXXV) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH(OH)\cdot CH_2\cdot CH_3$
(XXXVI) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH_3$, m. p. 125°
(XXXVII) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH(OH)\cdot CH_2\cdot CH_3$
(XXXVIII) $CH_3\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot CH_3$, m. p. 205°

The hexaene can be sublimed undecomposed in a high vacuum as lemon-yellow needles. It is the first synthetic purely aliphatic hydrocarbon with colour. It gives with antimony trichloride in chloroform an indigo-blue solution with an absorption band at 5980 A.

The new hydrocarbons are notable for the extreme sharpness of their absorption bands (Kuhn, *loc. cit.*).

## D. $HO_2C\cdot[CH{:}CH]_n\cdot CO_2H$ ($n = 1, 2, 3, 4, 5, —, 7$) *and* $HO_2C\cdot CH_2\cdot[CH{:}CH]_n\cdot CO_2H$ ($n = 1, 2, 3, 4$).

Until quite recently, muconic acid ($n = 2$) was the highest synthetic member of the polyene ωω′-dicarboxylic acid series. Crocetin and bixin are natural products of the same type with seven and nine conjugated double bonds respectively. They, however, contain four methyl groups as side chains. A procedure, discovered with Grundmann

(Kuhn and Grundmann, *Ber.*, 1936, **69**, 1757, 1979; 1937, **70**, 1318), has made it possible to prepare the symmetrical polyene dicarboxylic acids up to $n = 7$.

(XXXIX) $HO_2C{\cdot}CH{:}CH{\cdot}CO_2H$ (XL) $HO_2C{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO_2H$
(XLI) $HO_2C{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO_2H$
(XLII) $HO_2C{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO_2H$
(XLIII) $HO_2C{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO_2H$
(XLIV) $HO_2C{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO_2H$

One starts from the polyene moncarboxylic esters (XLV), which are condensed with potassium ethoxide and oxalic ester to oxalo-polyene carboxylic esters (XLVI). Lapworth (J., 1900, **77**, 1276) discovered this reaction for crotonic ester ($n = 1$), and Borsche (*Ber.*, 1932, **65**, 868; *Annalen*, 1933, **505**, 177) had already successfully applied it to sorbic ester ($n = 2$). It is noteworthy that, in the case of the higher esters, the condensation only proceeds in the presence of pyridine.

(XLV) $RO_2C{\cdot}CO_2R + CH_3{\cdot}[CH{:}CH]_n{\cdot}CO_2R$

$\downarrow$ KOEt, Py

(XLVI) $RO_2C{\cdot}CO{\cdot}CH_2{\cdot}[CH{:}CH]_n{\cdot}CO_2R$

$\downarrow$ $Ac_2O$

(XLVII) $RO_2C{\cdot}C(OAc){:}CH{\cdot}[CH{:}CH]_n{\cdot}CO_2R$

$\downarrow$ Al,Hg

(XLVIII) $RO_2C{\cdot}CH(OAc){\cdot}[CH{:}CH]_n{\cdot}CH_2{\cdot}CO_2R$

$\downarrow$ R'OH, NaOH

(XLIX) $R'O_2C{\cdot}[CH{:}CH]_{n+1}{\cdot}CO_2R'$

The oxalo-esters (XLVI) so obtained were acetylated with acetic anhydride, and the acetyl compounds (XLVII), which are derived from the enol forms, were reduced with aluminium amalgam. In accordance with Thiele's rule, they take up two hydrogen atoms at the ends of the conjugated system (XLVIII). The last stage is the removal of acetic acid (OAc and H from the ends of the chain !) by aqueous or alcoholic alkali. If the acetyldihydro-compound is treated with methyl-alcoholic alkali, the dicarboxylic acid (XLIX) is obtained as the dimethyl ester, and ethyl-alcoholic alkali yields the diethyl ester. Thus interchange of the ester groups occurs during the reaction. In this way one can pass from the monocarboxylic acids with $n$ double bonds to the dicarboxylic acids with $n + 1$ double bonds.

The synthesis of tetradecaheptaene-1 : 14-dicarboxylic acid ($n = 7$) did not follow the above scheme exactly. During the reduction of the acetyloxalo-ester $RO_2C{\cdot}C(OAc){:}CH{\cdot}[CH{:}CH]_6{\cdot}CO_2R$ with aluminium amalgam, the expected acetyldihydro-compound $RO_2C{\cdot}CH(OAc){\cdot}[CH{:}CH]_6{\cdot}CH_2{\cdot}CO_2R$ was not formed, but the dodecahexaene-1 : 12-diacetic ester $RO_2C{\cdot}CH_2{\cdot}[CH{:}CH]_6{\cdot}CH_2{\cdot}CO_2R$ was formed by replacement of the acetyl group by an atom of hydrogen. However, the polyene diacetic esters $RO_2C{\cdot}CH_2{\cdot}[CH{:}CH]_n{\cdot}CH_2{\cdot}CO_2R$ can be dehydrogenated to the polyene dicarboxylic esters by the action of atmospheric oxygen in the presence of alkali, a reaction found (Kuhn and Drumm, *Ber.*, 1932, **65**, 1458) for crocetin and bixin. We have made use of this in the synthesis of tetradecaheptaene-1 : 14-dicarboxylic acid, the formula of which differs from that of crocetin only in the absence of the four methyl side chains.

The oxalic ester method can also be applied to the *synthesis of methylated polyene dicarboxylic acids* (Kuhn and Grundmann, *Ber.*, **1937**, **70**, 1894). In this connection it may be observed that not only methyl groups, but also methylene groups at the ends of a conjugated system, will condense with oxalic ester. It is possible, therefore, to obtain one and the same compound in two different ways, accordingly as the "right" or the "left"

carboxyl group is introduced as oxalic ester. Thus β-methylmuconic acid (LII) can be prepared either from ββ-dimethylacrylic ester (L) or from β-ethylacrylic ester (LIV) as shown by the following formulæ. We obtained practically the same yields (36%) by both methods :

$RO_2C\cdot CO_2R + CH_3\cdot CMe{:}CH\cdot CO_2R$ (L) $\longrightarrow$ $RO_2C\cdot CO\cdot CH_2\cdot CMe{:}CH\cdot CO_2R$ (LI)

$\searrow$

(LII) $RO_2C\cdot CH{:}CH\cdot CMe{:}CH\cdot CO_2R$

$\nearrow$

(LIV) $RO_2C\cdot CH{:}CH\cdot CH_2Me + RO_2C\cdot CO_2R$ $\longrightarrow$ $RO_2C\cdot CH{:}CH\cdot CHMe\cdot CO\cdot CO_2R$ (LIII)

β-Methylhexatrienedicarboxylic acid (LVII) affords another example of this kind. Either β-methylsorbic ester (LV) or hexadiene-1 : 3-carboxylic acid ester (LIX) can be used as starting material, but the yields by the second route are very much better than by the first. In general, it appears that the course of the synthesis is rendered more difficult by β-methyl groups.

(LV) $RO_2C\cdot CO_2R + CH_3\cdot CH{:}CH\cdot CMe{:}CH\cdot CO_2R$

$\downarrow$

(LVI) $RO_2C\cdot CO\cdot CH_2\cdot CH{:}CH\cdot CMe{:}CH\cdot CO_2R$

$\downarrow$

(LVII) $RO_2C\cdot CH{:}CH\cdot CH{:}CH\cdot CMe{:}CH\cdot CO_2R$

$\uparrow$

(LVIII) $RO_2C\cdot CH{:}CH\cdot CH{:}CH\cdot CHMe\cdot CO\cdot CO_2R$

$\uparrow$

(LIX) $RO_2C\cdot CH{:}CH\cdot CH{:}CH\cdot CH_2Me + RO_2C\cdot CO_2R$

1 : 5-Hexatrienedicarboxylic acid (LXIII) was of especial interest on account of its connection with a metabolic product of geraniol. It was synthesised (Kuhn and Grundmann, *Ber.*, 1937, **70**, 1894) by the following route :

(LX) $CH_2Me\cdot CH{:}CH\cdot CHO + Zn + CHMeBr\cdot CO_2R$

$\downarrow$

(XLI) $CH_2Me\cdot CH{:}CH\cdot CH{:}CMe\cdot CO_2R$

$\downarrow$ $RO_2C\cdot CO_2R$

(LXII) $RO_2C\cdot CO\cdot CHMe\cdot CH{:}CH\cdot CH{:}CMe\cdot CO_2R$

$\downarrow$

(LXIII) $HO_2C\cdot CH{:}CMe\cdot CH{:}CH\cdot CH{:}CMe\cdot CO_2H$

$\downarrow$

(LXIV) $HO_2C\cdot CH{:}CMe\cdot CH_2\cdot CH_2\cdot CH{:}CMe\cdot CO_2H$

$\uparrow$

(LXV) $HO\cdot CH_2\cdot CH{:}CMe\cdot CH_2\cdot CH_2\cdot CH{:}CMe\cdot CH_3$

By complete reduction, introduction of two bromine atoms, and removal of two molecules of hydrogen bromide, the triene dicarboxylic acid (LXIII) was converted into 1 : 5-dimethylhexadiene-1 : 6-dicarboxylic acid (LXIV). This was identical with a dicarboxylic acid discovered by Hildebrandt (*Arch. exper. Path.*, 1907, **45**, 110) in the urine of dogs and rabbits fed with geraniol (LXV) or geranic acid (Kuhn, F. Köhler, and L. Köhler, *Z. physiol. Chem.*, 1936, **242**, 171).

This change in geranic acid in the animal organism appears to be analogous to that discovered by Verkade for fatty acids, and named by him ω-oxidation. These biological methods yield very much better results with the polyene carboxylic acids than with the fatty acids (Kuhn, F. Köhler, and L. Köhler, *ibid.*, 1937, **247**, 197). One cannot indeed feed the free acids, their salts or esters, but must use the amides, methylamides, anilides, etc. Kuhn and (Miss) Löw (unpublished work) have shown that, in the case of the fatty acids, such protection of the carboxyl group is of scarcely any value, since an amidase liberates the carboxyl group. The amides of the polyene carboxylic acids are, however, very stable against this enzyme.

Hexatrienedicarboxylic acid monoamide (LXVII) crystallises in a yield of 42% from the urine of rabbits which have received octatriene acid amide (LXVI). The former could be saponified with aqueous potash to the hexatriene-1 : 6-dicarboxylic acid (LXVIII).

(LXVI) $CH_3{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO{\cdot}NH_2$
(LXVII) $HO_2C{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO{\cdot}NH_2$
(LXVIII) $HO_2C{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO_2H$

The decatetraene acid amide (LXIX) yielded the *octatetraenedicarboxylic acid mono-amide* (LXX) in a yield of 20%. This was saponified to the yellow octatetraene-1 : 8-dicarboxylic acid (LXXI).

(LXIX) $CH_3{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO{\cdot}NH_2$
(LXX) $HO_2C{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO{\cdot}NH_2$
(LXXI) $HO_2C{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO_2H$

Yields up to 83% have been obtained in other cases. It appears from this work that, by using rabbits, preparative oxidations can be carried out, and that these are specific in their nature. Methyl is oxidised to carboxyl, but all double bonds in the molecule remain intact. The polyene dicarboxylic acids isolated from rabbit urine have been shown by mixed melting points to be identical with the corresponding dicarboxylic acids obtained by the oxalic ester synthesis.

The free oxalo-polyene carboxylic acids may readily be obtained by saponification of the oxalo-polyene carboxylic esters. These, like α-keto-acids in general, can be oxidised with hydrogen peroxide to the compounds with one carbon atom less. Grundmann (*Ber.*, 1937, **70**, 1148), who demonstrated this, thus obtained the following vinylene *homologues of glutaconic acid :*

(LXXII) $HO_2C{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CO_2H$
(LXXIII) $HO_2C{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO_2H$
(LXXIV) $HO_2C{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO_2H$
(LXXV) $HO_2C{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO_2H$

The absorption spectra of these compounds correspond exactly with those of the mono-carboxylic acids $CH_3{\cdot}[CH{:}CH]_n{\cdot}CO_2H$ with the same number of conjugated double bonds. The methylene group thus isolates the carboxyl completely from the chromophore. Glutaconic acid ($n = 1$) is very conveniently obtained in this way from crotonic ester, and also the dicarboxylic acid with $n = 2$ from sorbic ester. The latter acid has been shown to be identical with the piperylenedicarboxylic acid obtained by Willstätter (*Ber.*, 1895, **28**, 3271 ; 1898, **31**, 1535) by degradation of cocaine.

During the oxidation with hydrogen peroxide, removal of two carbon atoms also occurs to a small extent. One obtains from oxalosorbic ester not only piperylenedicarboxylic acid but also muconic acid. Thus it is possible by the indirect route of condensation with oxalic ester and subsequent oxidation with hydrogen peroxide to imitate *in vitro* the animal experiments of Dr. and Mrs. Köhler—the oxidation of methyl to carboxyl without affecting the double bonds present in the molecule.

## E. *Polyenes of the Terpene Group.*

Polyenes, whose carbon skeletons may be considered as built up of isoprene residues, occur in the pigments of the carotene group. The question naturally presents itself as to

how far the synthetic methods already known can be applied to the synthesis of such substances. The answer is that we are as yet only at the beginning of this field.

The aldol condensation of terpene aldehydes with other aldehydes by means of piperidine acetate and similar amine salts has been successful in several cases. For example, the condensation of citral (LXXVI) with acetaldehyde carried out by Kuhn, Badstübner, and Grundmann (*Ber.*, 1936, **69**, 98) yields citrylideneacetaldehyde (LXXVII) in very good yield.

$$\text{(LXXVI)}\ \mathrm{CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{:}CH{\cdot}CHO + CH_3{\cdot}CHO}$$
$$\downarrow$$
$$\text{(LXXVII)}\ \mathrm{CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CHO}$$

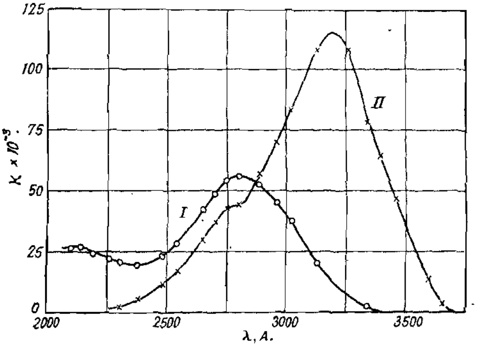
We are indebted to Heilbron and his collaborators for other important examples of this kind (*J.*, 1937, 755).

Especially noteworthy is the discovery of Fischer (*Ber.*, 1935, **68**, 1726) that β-methylcrotonaldehyde, first made available by him, condenses with itself under the same conditions as crotonaldehyde, forming the interesting dehydrocitral (LXXVIII) and farnesinal (LXXIX) :

$$\text{(LXXVIII)}\ \mathrm{2CMe_2{:}CH{\cdot}CHO \longrightarrow CMe_2{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CHO}$$
$$\text{(LXXIX)}\ \mathrm{CMe_2{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CHO}$$

From the formula for vitamin A (LXXXII) suggested by Karrer (*Helv. Chim. Acta*, 1931, **14**, 1431), it might be expected that the synthesis of the corresponding aldehyde

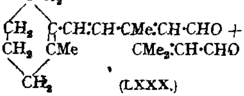
FIG. 2.

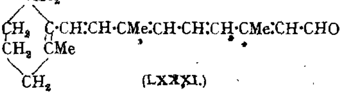



*I, β-Iononesemicarbazone.*
*II, β-Ionylideneacetaldehydesemicarbazone.*
*Solvent : ethyl alcohol.*

$$\kappa = \frac{2{\cdot}30}{c \times d} \log_{10} \frac{I_0}{I} \text{ (d in cm., c in mol./l.).}$$

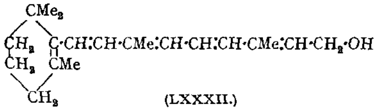
(LXXXI) could be carried out by condensation of β-ionylideneacetaldehyde (LXXX) with β-methylcrotonaldehyde :



We had already undertaken several unsuccessful experiments on the synthesis of the necessary β-ionylideneacetaldehyde. Dr. C. J. O. R. Morris, whom I am very pleased to see again this evening, was successful in solving this problem (Kuhn and Morris, *Ber.*, 1937, **70**, 853). By application of the chromous chloride method of v. Braun (*Ber.*, 1934, **67**, 269, 1735) to the *o*-toluidide of the already known β-ionylideneacetic acid, he was able to reduce the carboxyl group to an aldehyde group. The β-ionylideneacetaldehyde so obtained was characterised by a beautifully crystalline semicarbazone of melting point 194°. The absorption spectrum of this you see in Fig. 2 in comparison with that of β-iononesemicarbazone.

By condensation of the aldehyde with methylbutenal, and subsequent reduction by the Meerwein–Ponndorf method with aluminium *iso*propoxide, Morris obtained an oil, evidently a mixture of different alcohols. Among these was one which gave the blue colour with antimony trichloride in chloroform characteristic of vitamin A. The position of the absorption band was, as with the natural vitamin, at 6100 A., and a mixture of the natural and the synthetic compound could not be differentiated by chromatographic analysis. The synthetic alcohol (LXXXII) caused growth and healing of xerophthalmia with rats reared on a vitamin A-free diet.



(LXXXII.)

Since neither the natural nor the synthetic vitamin was pure, quantities which gave the same blue colour with antimony trichloride in chloroform were compared. In this way it was found that the growth effect of $0{\cdot}8 \times 10^{-6}$ g. of the synthetic alcohol corresponded with that of $0{\cdot}9 \times 10^{-6}$ g. of the natural vitamin A. Thus, not only the optical but also the biological properties show very close agreement.

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## 109. *The Electrochemistry of the Rusting Process along a Scratch-line on Iron.*

By R. S. Thornhill and U. R. Evans.

An apparatus is described which permits the measurement of electric currents passing around a scratch-line on iron covered with filter-paper soaked in bicarbonate solution; a fraction of the current is diverted through two nearly non-polarising electrodes to a galvanometer, and calibration on a second paper through which known currents are passed gives the relation between the galvanometer readings and the true current flowing through the first paper. The relation between the current and the corrosion produced suggests that the corrosion is mainly or wholly electrochemical. Ferrous ions are formed in the early stages, in amount corresponding approximately to the current passing; later, electrochemical oxidation of ferrous to ferric iron appears to set in, increasing the current in relation to the corrosion velocity.

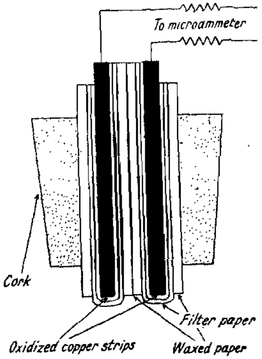
In previous papers (Evans, Bannister, and Britton, *Proc. Roy. Soc.*, 1931, *A*, **131**, 355; Evans and Hoar, *ibid.*, 1932, *A*, **137**, 343), the electric currents flowing between different regions of rusting iron were found to account quantitatively for the corrosion produced; but hitherto such tests have depended, directly or indirectly, on the cutting of the metal along the boundary of the anodic region. It would seem important to make a comparison between current and corrosion during natural corrosion *without cutting the specimen*, and an improved form of the apparatus introduced for detecting currents flowing around a scratch-line (Evans, *Nature*, 1935, **136**, 792) has made this possible.

When a single scratch-line is engraved on the surface of iron (previously exposed to air after abrasion), and a piece of filter-paper soaked in sodium bicarbonate solution of

suitable concentration is laid on to the surface, rusting will take place along the scratch-line, whilst the region around will remain free from corrosion. This simple distribution of attack requires the correct concentration of bicarbonate and a suitable form of iron. Concentrated solutions render the whole surface passive, probably because ferrous bicarbonate is sparingly soluble in concentrated sodium bicarbonate, and very dilute solutions produce attack at numerous other points; but at intermediate concentrations (usually 0·1—0·06N) the corrosion is confined to the most susceptible region, which, on iron of uniform quality, will usually be the scratch-line. The exact concentration needed to produce attack along the scratch-line depends on the previous history of the iron; the probability of corrosion diminishes with the length of pre-exposure of the scratch to air (Mears and Evans, *Trans. Faraday Soc.*, 1935, **31**, 532), and consequently a more dilute solution is needed to produce attack along a scratch-line which is not freshly engraved, increasing the danger of undesired corrosion elsewhere. A long period of storage between the abrasion of the whole surface and the production of the scratch-line is also found to necessitate an increased dilution, probably because the engraving of a scratch, whilst removing much of the air-formed oxide film, pushes down a portion into the groove—for which there is other evidence (Evans, Iron and Steel Institute Corrosion Committee, 5th Report, 1938).

The proper choice of iron is equally important if corrosion is to occur along the whole length of the scratch-line and not elsewhere. Carbonyl iron sheet, despite its purity, was found to be unsatisfactory, on account of either its softness or its slight porosity. The material chosen for the present experiments was the iron forming the basis of the "ferro-type" sheets used in photography, which contained C, 0·115; Mn, 0·35; Si, 0·045; S, 0·020; P, 0·072; Cr, 0·050%. This iron gave the desired distribution of attack, although the exact concentration required to confine attack to the scratch-line varied from sheet to sheet; the corrosion rate also varied, but this did not affect the object of the research, since the current generated by a given specimen was always compared with the corrosion produced on the *same* specimen. The sheets were abraded with French emery Hubert No. 3, and cut into squares 2·5 × 2·5 cm., which were kept in a desiccator for at least a week before being used. Even on this material, rust sometimes appeared at or near the cut edges of the squares; this could only be avoided by using concentrations so high that parts of the scratch-line failed to be attacked. The outlying regions of attack did not interfere with the measurement of the electric currents around the scratch-line, but they prevented the estimation of corrosion based on determination of the weight loss of the specimen, and it was necessary to estimate the attack by igniting the filter-paper after trimming off the rusty patches at the edges, and weighing the ferric oxide. This method of estimating corrosion was checked with the loss of weight of the specimen by means of separate experiments in which the out-lying rusted areas were *not* cut off, agreement being obtained to within the balance error; the greatest difference in seven experiments was ± 5%.

Fig. 1.



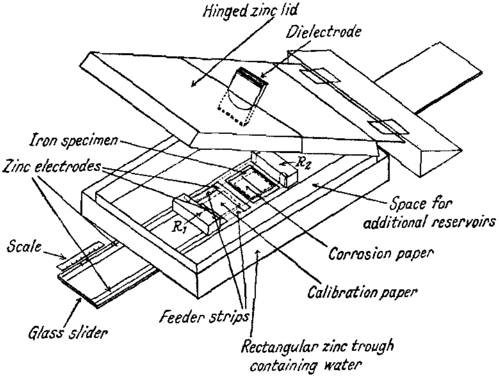

## Experimental.

*Apparatus.*—The electrical measurements depend on diverting through a galvanometer a *small fraction* of the current flowing along the wetted filter-paper, by way of a pair of copper–copper oxide electrodes (sufficiently free from polarisation for the purpose), so as to tap and return the current along two lines 2 mm. apart, the device being known as a "dielectrode." In constructing a dielectrode (Fig. 1), two strips measuring 6 × 2 cm. are cut from copper sheet previously abraded with Hubert No. 3. French emery, wiped with cotton-wool, and heated uniformly in a mildly oxidising gas-flame until the

last of the interference colours disappears. When cool, each is wrapped twice with a strip of filter-paper 2 cm. wide, a piece of waxed paper (2 × 6 cm.) is placed on each face, and the whole assemblage is joined together by applying wax along the longer edges. Two of the packs thus formed, placed face to face with the lower ends level, and fixed in position between two halves of a longitudinally cut cork, constitute a dielectrode. The current picked up by the dielectrode is measured by means of a Weston galvanometer Model 440 of 154 ohms resistance (1 divison = $0{\cdot}25 \times 10^{-6}$ amp.).

Since the fraction of current diverted by a dielectrode tends to vary with time, it is necessary to provide for continuous calibration against known currents. An essential condition for accuracy is that the paper along which the calibration currents are passed must be identical in " wetness " and concentration with the paper over which the natural corrosion currents are flowing. The calibration current is made to pass through a square of wet filter-paper, the electrodes being two L-shaped strips of zinc cemented to the waxed glass slider shown in Fig. 2. This filter paper (known as the " calibration paper ") must rest on a smooth wax surface, level

FIG. 2.




with the zinc electrodes. The calibration current is provided by an accumulator, joined to the two ends of a 140-ohm sliding resistance, so as to provide any *E.M.F.* between 0 and 2·0 volts ; it is measured with a Ferranti microammeter (250—0—250 microamps.), itself calibrated against other instruments. The iron square carrying the scratch-line is sealed into a depression in the wax, so that the filter paper covering it (known as the " corrosion paper ") is in the plane of the calibration paper. Both corrosion paper and calibration paper consist of Swedish filter-paper 2 cm. square. Two waxed celluloid boxes $R_1$ and $R_2$ are attached to the slider by wax and contain cotton-wool soaked in sodium bicarbonate solution. These serve as reservoirs, for both the calibration paper and the corrosion paper. To prevent evaporation, the specimen and reservoirs are enclosed in a flat zinc box ; the " lid " of the box, which carries the dielectrode, is fixed to a hinged frame and fits into a rectangular zinc trough forming a water-seal, so that the raising and lowering of the dielectrode through 3 mm. does not give access to the atmosphere. The humidity inside the box is maintained by two additional reservoirs containing moist cotton-wool; these are not shown in the diagram.

The two boxes $R_1$ and $R_2$, filled with sodium bicarbonate solution, are connected together by two feeder-strips of filter-paper running along the edges of the slider. The feeders are joined, when the specimen is in position, to the calibration and the corrosion paper by narrow fibres of filter-paper. When the dielectrode is not in use, it rests on a waxed celluloid bridge over which passes another strip of filter paper in contact with the feeder strips. This arrangement ensures (1) that the essential parts of the apparatus remain at the same degree of wetness throughout the experiment, and (2) that the soluble corrosion product, *i.e.*, ferrous bicarbonate, is not

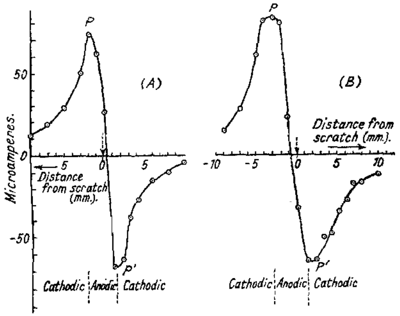
swept away from the scratch by liquid flowing between $R_1$ and $R_2$. (Such sweeping—which gave trouble in early experiments—can be practically eliminated by allowing an hour for the two reservoirs to come into hydrostatic equilibrium before an experiment is started.)

*Procedure.*—For each experiment, a square of iron is engraved with a single central scratch-line (parallel to the abrasion marks), with the Mears–Ward Machine (*J. Soc. Chem. Ind.*, **1934**, **53**, 382T) under a load of 500 g. The specimen is next fixed on the slider with wax, the calibration and corrosion papers, previously soaked in solution, are placed in position, and at least 5 minutes are allowed for the rust line to develop, before any readings are taken.

The dielectrode is first calibrated. A current of 20 microamps. is passed through the calibration paper, the dielectrode is brought down momentarily, and the deflexion of the galvanometer noted. The current is reversed, and the deflexion again noted. This is repeated in turn at + 40, — 40, + 60, — 60, + 40, — 40, + 20, — 20 microamps. In plotting a calibration curve, each galvanometer reading is corrected by deducting the mean of the two " zero readings " obtained with the dielectrode raised before and after the reading in question.

The variation of corrosion current with distance from the scratch is then measured by moving the slider forward 1 mm. at a time, the dielectrode being brought down in each position for just sufficient time to read the galvanometer; the mean of the two zero readings is deducted, as described above. In this way the whole specimen is traversed, first in one direction and then

Fig. 3.




in the other. The dielectrode is re-calibrated after each traverse. Some typical curves showing the distribution of current around the scratch-line are reproduced in Fig. 3; areas where the curve slopes downwards to the right are anodic, whilst those sloping upwards to the right are cathodic; the asymmetry, displayed in the curves published earlier (Evans, *Nature*, **1935**, **136**, 732), is found on some specimens, but not on all. Fig. 3*B* refers to the same square as 3*A*, but to a later stage of the corrosion; it will be noted that the anodic area tends to extend with time—a fact also indicated by the spread of the etched area on the metal.

During an experiment lasting one hour, three determinations are made of the current at the points (*P* and *P'*) between the anodic and the cathodic areas; in longer experiments, six determinations are made. By plotting these currents against time, an estimate of the total coulombs furnished is obtained.

After each experiment, the filter paper carrying the rust formed along the scratch-line is removed from the specimen and any subsidiary rust spots are cut off and rejected. Any loose or soluble product on the metal is wiped off with a second (smaller) piece of filter-paper. The two fragments of paper are left overnight in air containing ammonia vapour to precipitate any soluble iron compounds and are then washed free from sodium salts (colorimetric estimation of the iron in the wash-water with thiocyanate showed it to be about 0·00001 g., which can be neglected). The papers are then ignited in a silica crucible, cooled, and weighed on a balance sensitive to $10^{-5}$ g., Gauss's method being employed.

*Influence of Material chosen as Support for the Calibration Paper.*—Since at least part of the

current flows along the layer of liquid shut in *below* the calibration paper, it was feared that the material chosen as support might affect the thickness of this layer and consequently the relation between the galvanometer reading and the true current strength; this would vitiate the accuracy of calibration, since the calibration and corrosion papers *cannot* rest on the same material (the former *must* rest on a non-conductor, and the latter on iron). Accordingly, comparative experiments were carried out with calibration papers resting on four different bases, *viz.*, celluloid, wax, glass, and mica. The relation between the current flowing through the paper and that tapped through the galvanometer was found to be independent of the basis material (Fig. 4).

FIG. 4.

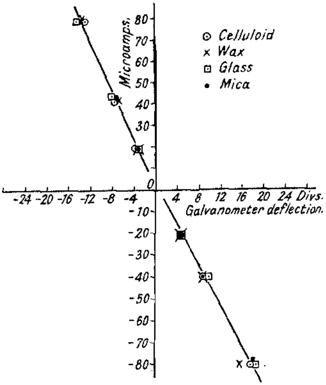
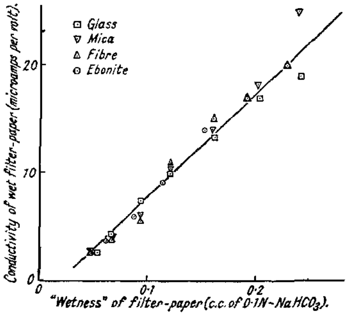



FIG. 5.




In other experiments the applied voltage $E$ was plotted against the current $i$ for various degrees of wetness of the strip as measured by the number of c.c. of bicarbonate solution dropped on it. When $i/E$ was plotted against wetness, the points for all the bases tested (fibre, ebonite, glass, and mica) followed the same straight line (Fig. 5). It was concluded that the basis material makes no serious difference to the measurements, and that the choice is one of convenience; in the actual experiments, wax was used.

*Influence of the Fraction of Current shunted through Measuring Circuit.*—The method of measurement involves the diversion of a certain fraction of the current which would otherwise flow through the corrosion paper; clearly, if this fraction is excessive the estimate of current obtained will differ from that which would be flowing had no diversion taken place. To ascertain whether the proportion shunted was too great, three sets of comparative experiments were conducted, each for 12 hours with 0·06N-sodium bicarbonate (*a*) with about 8% of the current shunted, and (*b*) with only about 4% shunted (this was obtained by introducing a resistance of 5000 ohms into the galvanometer circuit); the calibration curve of (*a*) was, of course, about half as steep as that of (*b*). The numbers obtained for the current (see Table) were, within the limits of accuracy, the same, suggesting that the shunting of current, up to 8%, does not greatly disturb the situation. It was, however, found inadvisable to keep the dielectrode in contact with the corrosion paper for longer than was absolutely necessary to obtain a reading; otherwise polarisation occurs.

*Comparison between the number of coulombs calculated when different fractions of the current were diverted.*

| | | |
|---|---|---|
| Added resistance of galvanometer circuit, ohms | Nil | 5000 |
| Fraction of current diverted, % | 8 | 4 |
| Experiment 1 | 1·08 | 1·13 |
| ,, 2 | 1·26 | 1·25 |
| ,, 3 | 1·13 | 1·12 |

*Time Limits of Accuracy of Experiment.*—As the amount of iron corroded by a scratch 2 cm. long is of the order of 0·1 mg. per hour, experiments lasting less than an hour will be inaccurate owing to the balance error. An upper time limit is fixed by the fact that in lengthy experiments the accumulation of rust will render the resistance of the corrosion paper slightly higher than that of the calibration paper, destroying the conditions requisite for accuracy. To ascertain when this error becomes serious, pieces of soaked filter-paper were placed for different times on squares of iron each bearing a scratch-line, and were then removed to a wax support and used as calibration papers. If the period of rusting was less than 40 hours, the same reading was obtained (for a given current) whether the dielectrode was brought down on the rust-line or elsewhere; but after longer periods, a slightly higher reading was obtained on the rust-line, because the increased resistance deflected an undue proportion of current through the measuring circuit. In actual experiments, the error would probably become perceptible somewhat earlier, because the test just described neglects the obstruction due to membranous rust extending across the liquid layer between filter-paper and metal, which is left behind when the filter-paper is transferred to the wax. It is believed, however, that for experiments not exceeding 12 hours, this particular error will be imperceptible.

A more serious error affecting long-continued experiments is caused by redeposition of iron as hydrated magnetite on the cathodic areas when the iron salts from the anodic areas reach these regions. Although paper soaked in bicarbonate on iron for periods up to 24 hours *without measurement of current* left no visible matter on the metallic surface, those in which the current had been measured often left a black or green stain on the cathodic region which cannot easily be removed by the ordinary cleaning methods, *e.g.*, cathodic treatment in citric acid (Evans and Hoar, *loc. cit.*, p. 346). Probably the slight pumping action produced when the dielectrode is brought down on to the filter-paper and raised again, helps the iron salts from the anodic scratch-line to reach the cathodic portions, and thus promotes partial redeposition. A similar dark mark is produced if a crystal of ferrous sulphate is placed on a piece of iron carrying a filter-paper soaked in sodium bicarbonate, whilst a black or dark green deposit is formed at the water-line on strips of iron partly immersed vertically in sodium bicarbonate. These deposits are almost certainly magnetite, partly hydrated, and their formation is easily understood. In the absence of iron salts, the only possible cathodic reaction is the deposition of hydrogen ions (or perhaps sodium ions), with immediate oxidation by atmospheric oxygen to water (and perhaps hydrogen peroxide) along with alkali. But when once iron ions have reached the cathodic area, they can also take part in the cathodic reaction, being similarly depolarised by oxygen to form oxides of iron. Once this has occurred in an experiment on iron engraved with a scratch-line, a deficiency of corrosion product in the filter-paper is to be expected. It is believed that this error is not appreciable in experiments that last less than 6 hours, certainly not in experiments lasting 3 hours.

## Results and Interpretation.

Fifty experiments were carried out in the three main series, the results being plotted in Figs. 6, 7, and 8; each point represents a separate experiment and is based on 20—40 different readings, involving the plotting of 6—12 calibration curves.

The experiments of Series A (Fig. 6) were conducted in the open laboratory. Correspondence between current and corrosion should not be affected by fluctuation of temperature in point of *time*, but inconstancy in point of *space* might possibly lead to "distillation" of liquid from one point to another, and thus disturb accuracy of calibration. Series B and C (Figs. 7 and 8) were therefore carried out in an air thermostat at 25°, and in Series C steps were taken to prevent the external air current from passing over the water in the water-seal, which might cause slight local cooling through evaporation. This final series was confined to experiments lasting for periods up to 3 hours, since it was desired to avoid the risk of the errors mentioned above, which affect long-period experiments; the experiments of series A and B included periods up to 12 hours.

Faraday's law indicates that one coulomb should correspond to 0·29 mg. of iron, if the anodic attack yields only *ferrous* salts, but only 0·19 mg. if *ferric* salts alone are produced, or if the *subsequent oxidation* of ferrous to ferric iron occurs as an electrochemical process. Most of the numbers lie between these limits (indicated by the oblique lines of Figs. 6, 7, and 8) or just outside them; the shorter experiments correspond to higher ratios of milligrams to coulombs than the longer ones. It is concluded that ferrous salts are formed in the early stages in amount corresponding almost quantitatively to the current passing,

but as the ferrous salts accumulate in the scratch-line, they become oxidised electrochemically to ferric salts, producing extra current so that the corrosion per coulomb diminishes.

Fig. 6.

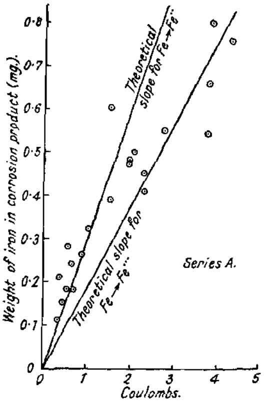



Fig. 7.

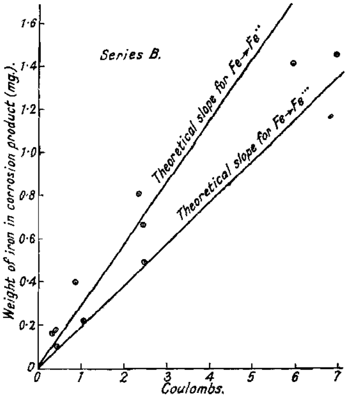
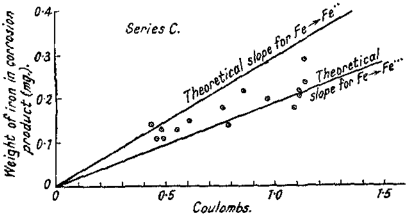



Fig. 8.




That current can be generated by the oxidation of ferrous compounds (at the anode) througl atmospheric oxygen (taken up at the cathode) is proved by experiments on the cell

Ag | $NaHCO_3$ (N/16); $FeSO_4$ (N/100) (air excluded) | $NaHCO_3$ (N/16); $Na_2SO_4$ (N/100) (air admitted) | Ag.

Three such cells furnished a current of 26—29 microamps. (falling gradually to 10—14 microamps. in 10·5 hours). This current must be produced by oxidation of the ferrous compound, since three "blank" cells,

Ag | $NaHCO_3$ (N/16); $Na_2SO_4$ (N/100) (air excluded) | $NaHCO_3$ (N/16); $Na_2SO_4$ (N/100) (air admitted) | Ag,

gave no measurable current during the same period. The anodic production of ferric iron was confirmed by the fact that the silver anodes removed from the three cells containing ferrous sulphate were found to be covered with a golden varnish-like film of ferric hydroxide

(the oxidation of 3 molecules of ferrous sulphate should give 2 molecules of ferric sulphate and one of ferric hydroxide).

The electrochemical formation of *ferric* compounds at a dissolving iron anode under conditions when the accumulating ferrous compounds were prevented from being swept away from the electrode was shown by W. J. Müller and Löw (*Z. Elektrochem.*, 1934, **40**, 575) to occur when the potential exceeded a certain value. Their experiments were made in cells fed with *current from an external source.* It has hitherto been assumed that in the cells present on *naturally corroding* iron (which *generate their own currents*), ferrous compounds are formed *electrochemically* and are then oxidised *chemically* by atmospheric oxygen to give rust. Doubtless this normally occurs, but, in the corrosion produced by soaked filter-paper on iron, the accumulation of ferrous products at the anode will be favourable for their electrochemical oxidation, and, by providing a surplus current, may lead to lower values for the ratio of milligrams to coulombs.

The measurements do not absolutely exclude the possibility of direct chemical attack on the metal in the early stages. If, for instance, it were assumed that ferric compounds were produced electrochemically from the outset, then the current would account for little more than half the total corrosion in the earliest stages. The fact that a rust-line appears in a few minutes actually shows that ferric compounds are formed in the early stages, but this is almost certainly due to the oxidation of ferrous compounds by the air. If it were to be assumed that ferric iron is exclusively produced by electrochemical action from the outset, it must also be assumed that there is less direct chemical attack on the metal in the later stages than in the early stages—which is extremely unlikely, since, as already stated, the attacked area extends with time. The rational explanation is that from the commencement the greater part of the attack is electrochemical, with the formation of ferrous compounds in the early stages and ferric compounds later. The high values for the shorter experiments in Series A and B were probably due to errors, since they were not obtained for corresponding periods in the more accurate experiments of Series C.

### CONCLUSION.

The corrosion occurring around a scratch-line on iron covered with bicarbonate-soaked paper appears to be *mainly or wholly electrochemical in character*, ferrous compounds being formed in the early stages, in amount roughly corresponding to the current passing; as these accumulate, they are oxidised electrochemically to ferric salts, increasing the amount of current in relation to the corrosion-rate.

We wish to express our thanks to the Department of Scientific and Industrial Research for a grant in aid of this research.

THE METALLURGICAL LABORATORIES, CAMBRIDGE UNIVERSITY. [*Received, January 28th,* 1938.]

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## 110. *The Polymerisation of Methylglyoxal.*

By L. de V. MOULDS and H. L. RILEY.

A study of the preparation and physical properties (refractive index, density, surface tension, and heat of combustion) of pure, dry, freshly distilled methylglyoxal and of both dry and wet polymerised samples has shown that the speed of polymerisation is greatly affected by traces of moisture. The results do not indicate the preferential formation of any particular polymer, but rather the progressive building up of structures of high molecular weight. Although methylglyoxal undoubtedly combines with water, the rate of polymerisation in the presence of water makes the isolation of a definite hydrate impossible.

METHYLGLYOXAL, when freshly prepared and dry, is a mobile volatile liquid. It polymerises, on standing, to a hard glass, more or less rapidly according to its purity. The factors affecting this polymerisation, though the subject of speculation, have not

hitherto been clearly understood. The polymerisation of glyoxal, the first member of the series of 1 : 2-diketones, has long been known to be affected greatly both in speed and in end-point by the presence of traces of moisture. If glyoxal is thoroughly dried by distillation from phosphoric oxide, the speed of polymerisation is slow, whereas the addition of a trace of moisture, or dissolution in solvents containing water, causes the instantaneous formation of paraglyoxal $(C_2H_2O_2)_n$ (Harries and Temme, *Ber.*, 1907, **40**, 167). Evaporation of a dilute aqueous solution of monomeric glyoxal brings about the formation of another polymer, polyglyoxal (Debus, *Annalen*, 1857, **102**, 205). Diacetyl, on the other hand, does not polymerise at an appreciable rate on standing, nor does water cause any change. Ice-cold potassium hydroxide solution slowly transforms it into a dimer (Diels, Blanchard, and Heyden, *Ber.*, 1914, **47**, 2357), whereas several days' shaking with cold concentrated hydrochloric acid gives a trimer.

During the preparation of methylglyoxal by oxidising acetone with selenium dioxide (Riley, Morley, and Friend, J., 1932, 1875), it was noticed that its speed of polymerisation, as indicated by its rate of setting to a hard glass, varied considerably and was apparently largely determined by the purity of the product. The above-mentioned properties of glyoxal and diacetyl suggest that methylglyoxal would behave in an intermediate manner and that its rate of polymerisation would be affected by traces of moisture, though probably not to the same extent as with glyoxal.

The preparation and properties of pure, anhydrous methylglyoxal have received little attention, most of the earlier workers being content to prepare either dilute aqueous solutions or only partly dehydrated compounds (compare, *inter alia*, v. Pechmann, *Ber.*, 1887, **20**, 3316; Harries and Turk, *ibid.*, 1905, **38**, 1632; Harries and Temme, *ibid.*, 1907, **40**, 172). Anhydrous, monomeric methylglyoxal was obtained by Meisenheimer (*ibid.*, 1912, **45**, 2635) and by Fischer and Taube (*ibid.*, 1926, **59**, 851) by distilling the polymer in a vacuum and passing the vapour over calcium chloride. This method of purification was employed in the present work, the crude methylglyoxal being obtained from acetone by the method of Riley, Morley, and Friend (*loc. cit.*). The product was an intensely yellow, mobile, volatile liquid, which polymerised only slowly if kept in a sealed tube, becoming of glycerol-like consistency in a fortnight and setting to a hard glass in about 10 weeks.

*Molecular Weight and Hydrates.*—The determination of the vapour density of methylglyoxal by Fischer and Taube (*loc. cit.*) indicated that the vapour was monomeric. The results of cryoscopic determinations in various solvents show discrepancies which are probably accounted for by differences in the extent of the polymerisation of the compounds used. The results of various workers are summarised in Table I, and this evidence

TABLE I.

| Description of material. | Solvent. | *M.* | Inferences. |
|---|---|---|---|
| Wet, polymerised | HOAc | 302 | Tetramer [1] |
| Dry, freshly distilled | $C_6H_6$ | 125 | Dimer [2] |
| ,, ,, | $H_2O$ | 72 | Monomer [2] |
| ,, ,, | $CHBr_3$ | 159, 122 | Dimer [2] |
| Dry, polymerised | $H_2O$ | 216 * | Trimer [3] |
| | | 88, 72 † | Monomer [3] |
| Wet, polymerised | HOAc | 680—730 | $8C_3H_4O_2,4H_2O$ [4] |
| ,, ,, | $H_2O$ | 131 | Dimer $(2C_3H_4O_2,2H_2O)$ [5] |
| ,, ,, | HOAc | 31 | Dissociated hydrate [5] |
| Dry, freshly distilled | $H_2O$ | 79 | Monomer [6] |
| ,, ,, | $C_6H_6$ | 70 | Monomer [6] |

* Immediately on dissolution. † One day later.

[1] Harries and Turk (*loc. cit.*). [2] Fischer and Taube (*Ber.*, 1924, **57**, 1506; 1926, **59**, 851). [3] Meisenheimer (*loc. cit.*). [4] Hahn and Schales (*Ber.*, 1934, **67**, 1816). [5] Bersin (*ibid.*, 1936, **69**, 560). [6] This paper.

suggests that pure freshly distilled methylglyoxal dissolves in water and in benzene in the monomeric condition, and that the dry polymerised variety slowly depolymerises in aqueous solution. The existence of the hydrates suggested by Hahn and Schales and by Bersin is open to doubt because of the indefinite nature of the wet polymerised

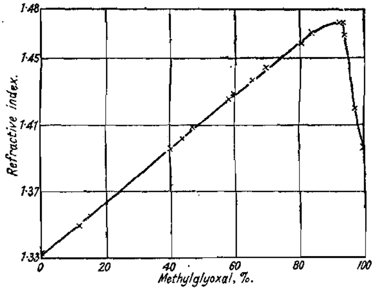
compounds employed. Dilute aqueous solutions of methylglyoxal are colourless when cold, but become green on warming, indicating the existence of an unstable hydrate in the cold aqueous solution, which dissociates at higher temperatures. Neuberg and Schou (*Biochem. Z.*, 1927, **191**, 469), from a study of the ultra-violet absorption spectrum, suggest the existence of a hydrate, probably $CMe(OH)_2{\cdot}CHO$, in aqueous solution.

*Refractive Indices of Methylglyoxal and its Aqueous Solutions.*—Pure, dry, freshly distilled methylglyoxal had $n_D^{25^\circ}$ 1·3327, compared with 1·3951 increasing to a constant maximum 1·4733 obtained by Fischer and Taube (*loc. cit.*) at 25°, and 1·4572 increasing to 1·4679 for the wet material found by Hahn and Schales (*loc. cit.*) at 20°. The refractive indices found for aqueous solutions of methylglyoxal are given in Table II. These values

Table II.

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Methylglyoxal, % by wt. | 0·0 | 11·57 | 40·24 | 43·91 | 47·14 | 58·42 | 59·66 | 59·70 | 65·62 |
| Mol.-fraction | 0·0 | 0·3163 | 0·1437 | 0·1637 | 0·1818 | 0·2599 | 0·2696 | 0·2703 | 0·3221 |
| $n_D^{25^\circ}$ | 1·3327 | 1·3491 | 1·3957 | 1·4019 | 1·4085 | 1·4259 | 1·4273 | 1·4290 | 1·4307 |
| Methylglyoxal, % by wt. | 69·72 | 80·53 | 83·72 | 92·51$_5$ | 93·72 | 93·77 | 97·19 | 100·00 | |
| Mol.-fraction | 0·3650 | 0·5081 | 0·5593 | 0·7553 | 0·7662 | 0·7837 | 0·8621 | 1·000 | |
| $n_D^{25^\circ}$ | 1·4438 | 1·4592 | 1·4658 | 1·4718 | 1·4721 | 1·4645 | 1·4200 | 1·3964 | |

are plotted against the percentage composition in the figure. The sharp maximum at 1·4721, which is in approximate agreement with the maximum reported by Fischer and




Taube (1·4733), occurs at the composition 93·5% methylglyoxal and 6·5% $H_2O$, corresponding to $C_3H_4O_2,0{\cdot}278H_2O$. This does not suggest the existence of a definite hydrate. It is also significant that when moist methylglyoxal is fractionally distilled in a vacuum, the purest fractions which can be obtained without passing the vapour over a dehydrating agent during distillation contain approximately $0{\cdot}25H_2O$.

The value $n_D^{25^\circ}$ 1·3327 gives $[R_L]_D$ 16·68 for the molecular refraction of monomeric methylglyoxal, whereas, on the basis of Eisenlöhr's atomic refractivities (*Z. physikal. Chem.*, 1911, **76**, 585), its enolic form should have $[R_L]_D$ 17·123 and its keto-form $[R_L]_D$ 16·076. The corresponding values for dimeric methylglyoxal are: *Found*, 33·36. *Calc.* for $CH_3{\cdot}CO{\cdot}CH(OH){\cdot}CH_2{\cdot}CO{\cdot}CHO$, 31·47; and for $CH_2{:}C(OH){\cdot}CH(OH){\cdot}CH{:}C(OH){\cdot}CHO$, 33·56. These values suggest the presence of both forms in the liquid.

*Density, Surface Tension, and Parachor.*—The determination of the density of methylglyoxal is complicated by its hygroscopic nature and tendency to polymerise. Precautions were taken to avoid the introduction of errors from these sources, and a value of 1·0383 was obtained; Fischer and Taube (*loc. cit.*) found 1·0455. As methylglyoxal contracts on polymerisation, and as this is accelerated by the presence of traces of moisture, it may be assumed *a priori* that the lower value is more nearly correct.

With similar precautions to exclude moisture and prevent polymerisation, surface-tension determinations gave a value of 28·05 dynes/cm. These values give the parachor of monomeric methylglyoxal as $[P] = 160{\cdot}2$ (Calc.: $[P] = 169{\cdot}2$, on Sugden's values for the atomic parachors; see "The Parachor and Valency," Routledge, London, 1930). For a dimeric methylgloxal $[P] = 320{\cdot}3$ (Calc.: 315·2). These results suggest that the dry, freshly distilled liquid is a mixture of the monomer and the dimer.

*Heat of Combustion.*—The method employed gave heats of combustion with a maximum error of $\pm 0{\cdot}3\%$. Dry, freshly distilled methylglyoxal at 20° exploded spontaneously when the oxygen pressure in the bomb used reached about 22 atm. This explosion occurred several times, once at an oxygen pressure of 19 atm., once at 25 atm., and ten times between 20 and 23 atm. In some cases the silica crucible employed was shattered. Spontaneous combustion did not occur with the wet or the dry polymerised sample. The explosions were probably due to peroxide formation. It is well known that aldehydes, ketones, alcohols, and ethers undergo auto-oxidation (cf. Milas, *Chem. Reviews*, 1932, **10**, 295), and Jorissen and van der Beek (*Rec. Trav. chim.*, 1926, **45**, 245) have isolated a peroxide formed during the auto-oxidation of benzaldehyde. Semenoff (*Chem. Reviews*, 1928, **6**, 347) has shown that peroxide formation in certain chain reactions under increased oxygen pressure may lead to explosions.

With methylglyoxal, peroxide formation may occur at both the ketonic and the aldehydic group, leading to the formation of an extremely unstable compound. That spontaneous combustion does not occur with the wet or polymerised samples is readily understood, for hydrate formation or polymerisation will occur at the active centres where peroxide formation occurs with the dry unpolymerised material. The results obtained are shown below.

| Description of sample. | Heat of combustion, kg.-cals./g.-mol. |
|---|---|
| Dry, freshly distilled | 344·9 |
| Dry, 11 weeks old, vitreous | 337·3 |
| $C_3H_4O_2,\frac{1}{3}H_2O$, polymerised, vitreous | 331·1 |
| $C_3H_4O_2,\frac{2}{3}H_2O$, polymerised, very viscous | 330·0 |
| $C_3H_4O_2,H_2O$, polymerised, very viscous | 328·9 |

The following values for the heat of combustion of methylglyoxal (in kg.-cals./g.-mol.) have been obtained by previous workers: 330 (v. Euler and Linder, "Chemie der Hefe und der alkoholischen Gärung," p. 248, Leipzig, 1915, indirect estimation); 333·7 (Aubel, *Compt. rend.*, 1926, **183**, 573, by calculation, the heat of formation being assumed to be 86); 326 (Fromageot and Emami, *Bull. Soc. chim.*, 1931, **49**, 929, by an indirect method); 345·7 (Neuberg and Hoffman, *Biochem. Z.*, 1932, **252**, 440). The last value was obtained from dry, freshly distilled methylglyoxal prepared by the method of Fischer and Taube (*loc. cit.*), and agrees well with the value obtained in the present investigation.

The values for the heat of combustion given above indicate that the pure, dry, freshly distilled methylglyoxal undergoes a slow polymerisation involving the evolution of approximately 8 kg.-cals. in the course of 11 weeks. The substance containing $\frac{1}{3}H_2O$, which sets rapidly to a vitreous solid, has a heat of combustion 6·2 kg.-cals. less than the dry vitreous variety. This further decrease in the heat content is due either to more extensive polymerisation or to hydrate formation, or possibly to both these factors. It is perhaps adventitious that the further decrease in the heat content shown by the sample containing an additional $\frac{2}{3}H_2O$ is exactly twice the decrease shown by the sample containing an additional $\frac{1}{3}H_2O$, and it would be unwise, owing to the complicated nature of the system, to conclude from this that the heat of hydration of methylglyoxal is 3·3 kg.-cals. The results suggest, however, that the heat effect of hydration will be of this order.

Although methylglyoxal forms an azeotropic mixture with water of the approximate composition $C_3H_4O_2,0{\cdot}28H_2O$, and although hydrates do undoubtedly exist in the liquid phase at room temperature of sufficient stability to be undecomposed by calcium chloride, yet the rapid polymerisation which occurs in the presence of water makes the isolation of any definite hydrate impossible. The preparation of monomeric, or only slightly polymerised methylglyoxal is possible by careful exclusion of water in the final stages and

by the vapour phase dehydration with calcium chloride during distillation. The use of phosphoric oxide is not recommended, as this causes sufficient decomposition to introduce appreciable amounts of water into the product. Even the dry material polymerises slowly, possibly owing to the presence of minute traces of water. This, and the fact that the addition of water brings about a pronounced increase in the rate of polymerisation, suggests that the mechanism of the process is as follows:

$$2CH_3\cdot CO\cdot CHO + 2H_2O \longrightarrow 2CH_3\cdot CO\cdot CH{<}{\begin{smallmatrix}OH\\OH\end{smallmatrix}} \longrightarrow \begin{matrix}CH_3\cdot CO\cdot CH{<}^{OH}\\ \phantom{CH_3\cdot CO\cdot CH}{>}O\\ CH_3\cdot CO\cdot CH{<}_{OH}\end{matrix} + H_2O, \text{ etc.}$$

The rapid polymerisation of glyoxal itself, and the fact that diacetyl does not polymerise, suggest that the aldehyde group and not the ketone group is the active centre in bringing about the polymerisation of methylglyoxal. The formation of a hard glass suggests the presence of cross linkages in the polymerised substance. These are possibly formed through the agency of polymers such as $CH_3\cdot CO\cdot CH(OH)\cdot CH_2\cdot CO\cdot CHO$.

The results do not indicate the preferential formation of any particular polymer, but rather the progressive building up of structures of high molecular weight. The physical constants indicate the presence of both keto- and enolic forms in the unpolymerised liquid.

## EXPERIMENTAL.

Crude methylglyoxal was prepared by the method described by Riley, Morley, and Friend. A fraction (50 c.c.) of fairly pure methylglyoxal boiling at 103—110° at atmospheric pressure, which was initially a mobile liquid and in the course of ½ hour after distillation had become very viscous with the evolution of considerable heat, was dissolved in dry ether and dried for 24 hrs. over sodium sulphate. After removal of solvent, the residue was distilled in a vacuum, and a fraction, b. p. 57—60°/20 mm., collected, the receiver being cooled in liquid air. On warming the receiver to room temperature, it was seen in some preparations to contain two layers, the uppermost being more mobile and yellow. This was poured off, and in 2 days it set to a hard glass. Typical analyses of different specimens were: C, 47·3, 47·7, 47·0; H, 6·1, 5·8, 5·9 (Calc. for $C_3H_4O_2,\frac{1}{4}H_2O$: C, 47·0; H, 5·9%). The separation into two layers was probably connected with the effect of traces of water on the rate of polymerisation. The lower layer had a similar composition to the upper. The residual water could not be removed by dehydration of the liquid or its ethereal solution with sodium sulphate, potassium carbonate, calcium chloride, or phosphoric oxide. The use of the last two reagents diminished the yield. The best results were obtained by distilling the above fraction under very low pressure, passing the vapour over calcium chloride granules, freshly dried at 260°, and condensing the distillate by means of liquid air. The distillation was repeated twice, the final product being a yellow, mobile, pungent liquid. It remained so for 3 days after distillation; it then gradually became less mobile, and in 3 weeks it had the consistency of glycerol; in 6 weeks it flowed very slowly, and in 10 weeks it had set to a hard glass comparable with that given by $C_3H_4O_2,\frac{1}{4}H_2O$. During this time the colour changed from deep yellow to greenish-yellow. The glass dissolved in many organic solvents giving green solutions, and in water giving a colourless solution (Found: C, 49·8, 49·4; H, 5·6, 5·55. Calc. for $C_3H_4O_2$: C, 50·0; H, 5·6%).

The molecular-weight determinations were made by Beckmann's cryoscopic method in benzene and water, a freshly distilled sample of the methylglyoxal being used.

The refractive indices were determined by means of an Abbé refractometer, the prisms being at 25° ± 0·25°. The mixtures of water and methylglyoxal were made up in a small weighing bottle. Care was necessary in making up the mixture containing 7% $H_2O$ as this set rapidly to a hard glass with considerable evolution of heat. If the water was added quickly the mixture boiled very vigorously.

The density determinations were carried out by distilling the sample directly into a small specific gravity bottle cooled in liquid air. The bottle was then placed in a test-tube and allowed to attain a temperature of 25° in a thermostat, care being taken to prevent the access of moisture. A check determination was carried out on a sample of pure benzene.

The surface tension of freshly distilled methylglyoxal was determined at 25° by the capillary rise method, precautions being taken to exclude every trace of moisture.

A Mahler–Kroecker bomb, kindly lent by Dr. J. H. Jones, of the Coal Survey Laboratory (D.S.I.R.), King's College, Newcastle-upon-Tyne, was employed in determining the heats of

combustion of the various samples of methylglyoxal. Ignition was effected by 1" of cotton thread fastened to a piece of platinum wire connected to the two electrodes and dipping into the sample in the crucible. The heat of combustion of the cotton (11 cals.) was allowed for. Check determinations using medicinal paraffin were carried out. Because of the vigorous manner in which pure, dry methylglyoxal burns, incomplete combustion may occur, due to the scattering of the sample. Fischer and Taube (*loc. cit.*) had noted this. To overcome this difficulty, about 0·5 g. of the sample was weighed from a well-stoppered weighing bottle into the bomb crucible and immediately covered with a similar amount of medicinal paraffin. This was placed in the bomb, which was then screwed up, all these operations being carried out as rapidly as possible. The mixture burned completely in an oxygen pressure of 18 atm. A standardised Beckmann thermometer was used, and the usual cooling corrections were employed.

KING'S COLLEGE (UNIVERSITY OF DURHAM),
NEWCASTLE UPON TYNE. [*Received, March 5th*, 1938.]

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## 111. *Properties of the Oxides of Nitrogen. Part VII. Flame Propagation in the System Dinitrogen Pentoxide–Ozone.*

By (the late) T. M. LOWRY and R. V. SEDDON.

By spectrographic means it has been proved that the unstable dinitrogen hexoxide is present in a mixture of the pentoxide (nitric anhydride) and ozone undergoing slow decomposition and also in the flame-front in the explosive reaction of these gases. The kinetics of the slow reaction have been stndied, and the mechanism shown to involve successively the unimolecular decomposition of the pentoxide, the reaction of ozone with the products, a bimolecular reaction of nitrogen trioxide formed in both the previous steps, and then the re-formation of dinitrogen pentoxide. The mechanism of the explosive reaction is exactly the same, the sequence of reactions proceeding at such a rate as to be adiabatic and self-propagating.

THE results of the detailed study of the explosive reaction between dinitrogen pentoxide and ozone (Part VI, J., 1937, 1461) showed that the flame is propagated by the diffusion of "hot" molecules from the flame-front into the unburnt gases, causing activation and further reaction.

The present paper deals with the actual reactions taking place in the flame-front, and by spectrographic means we have now proved that the unstable intermediate compound, nitrogen trioxide, is present both in the flame-front and in the mixture of nitric anhydride and ozone. A detailed study of the rate of the slow decomposition of the latter in the presence of the former has now shown it to be proportional to the two-thirds power of the concentration of each reactant. This, together with other results, supports the mechanism for the reaction suggested by Schumacher and Sprenger (*Z. angew. Chem.*, 1929, **42**, 627), in which the primary reaction is the decomposition of the pentoxide, the products combining with ozone to form nitrogen trioxide, which immediately decomposes bimolecularly. The dinitrogen pentoxide is continually re-formed, and the concentration remains constant.

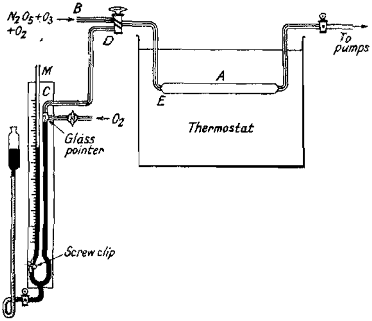
When the gas mixture is raised to a sufficiently high temperature it inflames, and the sequence of reactions, which is the same as in the slow process, becomes continuous, the energy liberated in the bimolecular decomposition of the trioxide causing further decomposition of dinitrogen pentoxide and resulting in a thermal energy chain mechanism. This conclusion differs slightly from that stated in our previous paper, in that the thermal energy required to propagate the reaction is drawn, not from the excess energy carried by the diffusing "hot" trioxide, but from the energy liberated in the exothermic bimolecular decomposition of nitrogen hexoxide.

### EXPERIMENTAL.

*The Slow Reaction between Dinitrogen Pentoxide and Ozone.*—The apparatus is shown in Fig. 1, and for comparison with the results for the flame, the reaction vessel *A* was made from the same sample of soda glass and of the same shape as those used in the work on the flame.

The first tube used had an internal diameter of 13·6 mm. and a volume of 37·5 ± 0·5 c.c. Before use, the tube was washed with concentrated nitric acid, water, and then methylated spirit, and dried in a current of air. After being sealed on to the apparatus the tube was washed out with dry oxygen and allowed to stand overnight full of oxygen. The apparatus was connected at *B* to the mixing bulb, and immediately after admission of the gases to the reaction vessel the latter was connected to the mercury manometer *M*. The space above the mercury from *C* to *D* was filled with oxygen, and the pressure at the beginning was so adjusted that, on connecting the reaction vessel and the manometer, oxygen was forced into the capillary *D* to *E*. The oxygen provided adequate protection for the mercury against the corrosive action of the gas mixture. The reaction results in the decomposition of ozone with consequent increase in pressure according to the equation : $2O_3 = 3O_2$. This increase of pressure was measured on the left-hand tube of the manometer, the mercury in the right-hand tube being kept at a fixed height, indicated by a glass pointer, by means of a screw clip on the rubber connection between the right- and the left-hand tube. The thermostat temperature was constant to 0·01°.

FIG. 1.




*Variation of Rate of Decomposition of Ozone with Partial Pressure of Dinitrogen Pentoxide and Ozone.*—Typical curves for the increase of pressure with time are shown in the lower part of Fig. 2. In the upper part of the figure the gradients of the pressure–time curves are plotted against time, and the exact initial rate of decomposition of ozone is obtained by extrapolation to zero time.

The rate of decomposition of ozone, expressed as the number of mm. decomposed per minute, is plotted against the partial pressure of the pentoxide in Fig. 3. The initial pressure of ozone in the mixing bulb was 50 mm., and the total pressure in the reaction vessel was 700 ± 2 mm. The curve in Fig. 3 is for the expression :

$$\text{Rate} = 0{\cdot}15 p_{N_2O_5}^{2/3}$$

and the experimental values denoted by crosses follow this very closely; hence the rate is proportional to the two-thirds power of the partial pressure of dinitrogen pentoxide.

The logarithm of the rate of decomposition is related linearly to that of the partial pressure of ozone when the pentoxide pressure is constant. The gradients of these straight lines for several pressures of pentoxide are given in the following table. The average gradient is 0·63; therefore :

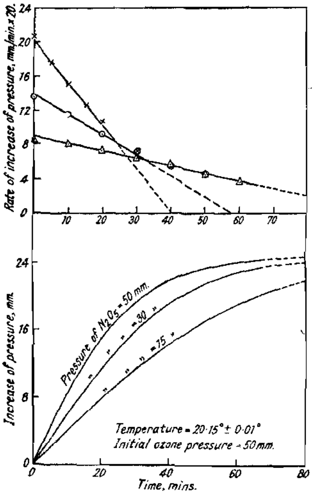
$$-\,d[O_3]/dt = K[O_3]^{0{\cdot}63}$$

| $N_2O_5$ pressure, mm. | 10 | 20 | 25 | 30 | 35 | 40 | |
|---|---|---|---|---|---|---|---|
| Gradient | 0·62 | 0·66 | 0·62 | 0·60 | 0·645 | 0·625 | Mean 0·63 |

*Variation of Rate of Decomposition with Temperature.*—The initial rate was studied over the temperature range 20—45°. At higher temperatures the mixture inflamed when admitted to the reaction tube. From the results, the activation energy was calculated to be 19,720

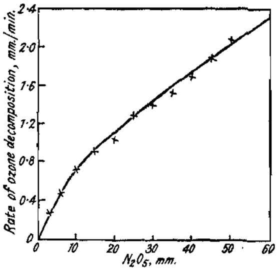
cals., and the Arrhenius law is obeyed over the whole range of temperature. It was observed that at 40° and 45°, when all the ozone has been decomposed and the rate of decomposition of the pentoxide is appreciable, the pressure–time curves for the decomposition of ozone in the presence of the pentoxide do not become horizontal, but pass gradually into the straight-line curves for the decomposition of the latter alone. This suggests that the rate-controlling process in the decomposition of ozone is the unimolecular decomposition of the pentoxide, which is catalysed to a certain extent by the ozone, and the apparent decomposition of ozone is due to the combination of this with the decomposition products of the pentoxide. This view is supported by the results described above.

FIG. 2.



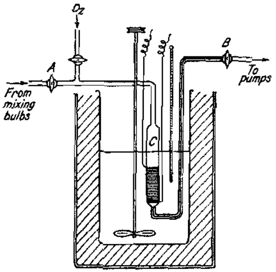

*Rate of decomposition of ozone.*

FIG. 3.




*Rate of decomposition of ozone in presence of nitric anhydride.*

FIG. 4.

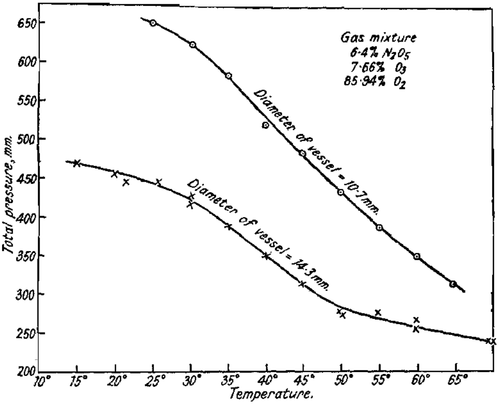



*Effect of Increased Surface on the Initial Rate.*—The reaction tube was packed with glass rods, the surface/volume ratio being increased 7·2 times. The rate of reaction was increased by only 2—3%. Other experiments in which vessels of very narrow diameter were used gave a similar result; *e.g.*, no difference in velocity could be detected in tubes of 5·4 and of 13·7 mm. diameter. The results show that the reaction between the pentoxide and ozone is almost entirely homogeneous, and that if it is a chain reaction the chain carriers are unaffected by diffusion to the walls of the containing vessel.

*Variation of Ignition Temperature with Pressure.*—The apparatus is shown in Fig. 4. A soda-glass tube, of 14·3 mm. diameter, was wound at its lower end with a nichrome heating coil. This was used for heating a constant-temperature bath of liquid paraffin. The bath was well stirred with a glass propeller, and its temperature could be kept constant to within 0·1° for several minutes. A big-bore stopcock *A* was used for admitting the gas mixture rapidly. The method was to get the bath to a suitable temperature, prepare a mixture containing 30 mm.

of dinitrogen pentoxide and 50 mm. of ozone, close stopcock *B*, and 10 mins. after the mixing of the gases had started, to admit them to *C* as rapidly as possible by opening *A*. If the conditions were suitable, the mixture inflamed at the bottom of the tube and the flame moved upwards. The reaction vessel *C* was evacuated, washed with oxygen, and another admission made 2 mins. after the first. This was continued at 2-min. intervals until two successive admissions gave no flame, *i.e.*, the critical pressure had been reached. This was repeated using higher temperatures and beginning with lower pressures of the mixture of same percentage composition. A reaction vessel of diameter 10·7 mm. was also used. The curves for the variation of ignition temperature with pressure are shown in Fig. 5.

FIG. 5.




*Variation of ignition temperature with pressure.*

*The Stationary Flame.*—In order to study the flame spectrographically, a stationary flame was obtained in a vertical tube of 5 mm. diameter by passing in a mixture of the pentoxide and ozonised oxygen at the bottom, and balancing the rate of admission against the rate of consumption of reactants at the flame-front. The flame could be held at any point for several minutes. It was observed that the tube became quite warm near the flame-front, but attempts to detect long-wave emission by means of infra-red and hypersensitive panchromatic plates were unsuccessful.

*Absorption Spectrographs of the Flame and Gas Mixture.*—An ordinary glass prism instrument with small dispersive power was used with hypersensitive panchromatic plates. A 25-watt, 220-volt lamp covered by four pieces of parchment was used as a source of light, and placed 3 feet away from the slit, which was 4 × 0·05 mm. The stationary flame-front was held in front of the slit, and short exposures of not more than 60 secs. made. The absorption spectrum appeared as a series of dark bands down the centre of each photograph, and the wave-lengths of the main bands were measured by comparison with a neon spectrum taken on the same plate. The photograph of the spectrum of the gas mixture was obtained by using a horizontal tube 82·5 cm. long, with a continuous stream of dinitrogen pentoxide and ozonised oxygen passing through it. The measurements for the flame and the gas mixture are recorded below. They compare favourably with measurements made by Warburg and Leithauser (*Sitzungsber. K. Akad. Wiss. Berlin*, 1907, 229) on a mixture of the pentoxide and ozone.

| Spectrum. | Wave-lengths of main bands, ± 4 A. | Spectrum. | Wave-lengths of main bands, ± 4 A. | Warburg and Leithauser's measurements. |
|---|---|---|---|---|
| Flame-front | 6650—6593 | Mixture of $N_2O_5$, $O_3$, and $O_2$ | 6650—6598 | 6640—6600 |
| | 6310—6209 | | 6310—6208 | 6300—6220 |

The wave-lengths of the main bands for the flame-front and the gas mixture are identical. These bands are undoubtedly due to the presence of nitrogen trioxide; hence the blue flame-front and the reacting mixture contain this higher oxide of nitrogen. Warburg and Leithauser showed that dinitrogen hexoxide is only present to the extent of 1% in a mixture of 60 mm of the pentoxide and 60 mm. of ozone. In the flame-front the concentration of hexoxide will be high, for probably the whole of the pentoxide has reacted with ozone.

## Discussion.

The spectrographic investigation of the flame-front and the gas mixture showed that nitrogen trioxide, $NO_3$, is present in each case, and no doubt is the intermediate product in the slow pentoxide-catalysed decomposition of ozone and in the explosive reaction between the last two reagents.

The results on the slow reaction show that the rate of decomposition of ozone is proportional to the two-thirds power of the concentration of each reactant; *i.e.*,

$$-\,d[O_3]/dt = k[N_2O_5]^{\frac{2}{3}}[O_3]^{\frac{2}{3}}.$$

This supports the mechanism for the reaction suggested by Schumacher and Sprenger (*loc. cit.*). The primary process is the simple decomposition of dinitrogen pentoxide, followed by two reactions which they assume to constitute a chain process, then the regeneration of the pentoxide from the products:

(1) $N_2O_5 = NO_2 + NO_3$ $(k_1)$ (3) $NO_3 + NO_3 = NO_2 + NO_2 + O_2$ $(k_3)$
(2) $NO_2 + O_3 = NO_3 + O_2$ $(k_2)$ (4) $NO_2 + NO_3 = N_2O_5$ $(k_4)$

Here $k_1$, $k_2$, etc., are the rate constants for the forward reactions. On the basis of this assumed mechanism they derived the following theoretical expression for the rate of decomposition of ozone:

$$-\,d[O_3]/dt = k_3\sqrt[3]{(k_1k_2[O_3][N_2O_5]/k_3k_4)^2}$$

in agreement with our experimental result. The primary process, *i.e.*, the decomposition of dinitrogen pentoxide is well known to be a homogeneous reaction, which agrees with our observation that increase of surface does not affect the rate appreciably. Since the rate is slightly *increased* by packing the reaction tube or removing the inert gas (see Part VI, *loc. cit.*, p. 1466), the rate-controlling reaction must be unimolecular.

In 1884 van 't Hoff suggested that explosion in an exothermic reaction results from rapid acceleration in rate of reaction due to progressive self-heating. The idea has been further developed by Semenoff and a formula evolved for the relationship between critical explosion temperature and pressure, *viz.*, $\log_{10} P/T = A/T + B$, where $A = (E/2\mathbf{R}) \log_{10}e$, and $B$ depends on the composition of the gas mixture and the diameter of the vessel. From the results recorded in Fig. 5, linear relationships were obtained when $\log_{10} P/T$ was plotted against the reciprocal of absolute temperature, and $A$, the gradient of the straight lines, was found to be 1160 and 800. Calculated from the activation energy, $A$ is 2170, *i.e.*, of the same order. The agreement with the theory is satisfactory in view of the complications involved in the method of measuring the ignition temperature. Semenoff showed that this relationship between pressure and temperature is obeyed whether the mechanism of explosion involves branching chains or is purely thermal. As will be shown later, we incline to the hypothesis of a purely thermal initiation in which "ignition depends upon heating a sufficient volume of gas to a sufficient temperature" (Taylor-Jones, "Induction Coil Theory and Applications").

The mechanism of the flame is the same as for the slow reaction, except that the processes involved are so rapid as to be adiabatic and self-propagating. The molecules of the unstable intermediate product, nitrogen trioxide, formed by the decomposition of dinitrogen pentoxide and by the combination of nitrogen dioxide and ozone, diffuse forward and combine to liberate thermal energy which serves to ignite the layer of gases in front. Nitrogen trioxide may also be decomposed by collision with a molecule of ozone. This is probable, for approximately 2 mols. of ozone are used up for 1 mol. of pentoxide to give a maximum flame speed (see Part VI, *loc. cit.*, p. 1465).

The complete mechanism of the flame is represented as follows:

(5) $N_2O_5$ + thermal energy = $NO_2 + NO_3$
(6) $NO_2 + O_3 = NO_3 + O_2$
(7) $NO_3 + NO_3 = NO_2 + NO_2 + O_2$ + thermal energy
(8) $N_2O_5$ + thermal energy = $NO_2 + NO_3$, etc.
also (9) $NO_3 + O_3 = NO_2 + 2O_2$.

The mechanism undoubtedly involves the initial formation of the unstable intermediate product, mononitrogen trioxide.

All the phenomena are typical of a flame and can be explained on the basis of a simple kinetic theory. Propagation of the flame is by diffusion of trioxide molecules from the flame-front into the unburnt gases, followed by a bimolecular reaction of those trioxide molecules in which sufficient thermal energy is liberated to ignite the layer of unburnt gases in front. The velocity of the flame is largely determined by the rate of diffusion of the trioxide molecules, as has been shown by the results of Part VI (*loc. cit.*).

The sequence of reactions taking place in the explosive and in the slow combination of dinitrogen pentoxide and ozone is essentially the same, but in the former the reactions proceed at such a rate as to be adiabatic and self-propagating.

We are indebted to Professor R. G. W. Norrish for many helpful discussions, and to Imperial Chemical Industries, Limited, for grants for maintenance and apparatus.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, February 12th*, 1938.]

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## 112. *The Retardation of Chemical Reactions. Part VIII. The Darkening of Alkaline Solutions of Sodium Salicylate.*

By JOHN HILTON and KENNETH C. BAILEY.

The object of this investigation is to examine the dark brown colour which develops rapidly in alkaline solutions of sodium salicylate (used in the treatment of muscular rheumatism and similar complaints), to survey the means already suggested for retarding the development of the dark colour, and if possible to discover other means.

It is found that the darkening of these solutions is due to absorption of atmospheric oxygen, and not of ammonia. Retardation by anti-oxygens has been investigated. Sodium thiosulphate (0·1%) and thiourea (0·04%) are suggested as the most suitable retarders when the salicylate solutions are to be used for medicinal purposes.

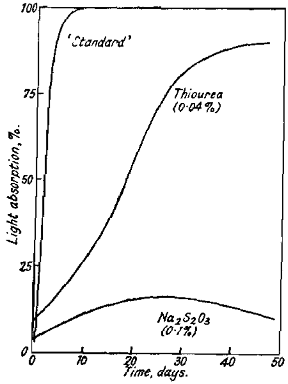
*The Cause of the Darkening.*—The "standard" alkaline salicylate solution used contained 5% of sodium salicylate and 2·5% of sodium bicarbonate in water.

That the change in colour is due to auto-oxidation of the salicylate seems probable, in view of the ready oxidation, with colour change, of alkaline solutions of pyrogallol and other phenolic materials. This has been the opinion of most workers (Greenish and Beesley, *Pharm. J.*, 1915, **94**, 201; Grill, *J. Amer. Pharm. Assoc.*, 1932, **21**, 763; Beukema-Goudsmit, *Pharm. Weekblad*, 1934, **71**, 196; Liberalli, *Boll. Assoc. brasil. farm.*, 1935, **16**, 154). On the other hand, Macadie (*Pharm. J.*, 1915, **94**, 355) attributed the darkening to the absorption of traces of ammonia from the air. Addition of ammonia to an alkaline salicylate solution certainly causes a fairly rapid darkening, even when the solution is sealed off from the air, but the colour is redder than the normal. The authors have found that (*a*) a solution of salicylate and bicarbonate in air-free water, exposed to nitrogen, does not darken, and (*b*) a solution of the same reagents in ammonia-free water (checked with Nessler's reagent), and exposed only to air freed from any traces of ammonia by passage through sulphuric acid, darkens at a normal rate. It seems certain that oxygen, not ammonia, is responsible for the change.

Martins (*Tribuna farm.*, 1934, **3**, 8, 30) suggests that the oxidation is brought about by

an oxidase, pointing out that, although certain substances (see later) retard the normal darkening, they do not prevent oxidation by hydrogen peroxide. He concludes that their action is antiseptic rather than anti-oxygenic. This reasoning is unsound, for anti-oxygens of the usual types, although very effective in checking oxidation by oxygen gas, are generally unable to arrest oxidation by more vigorous oxidising agents. A solution of sodium salicylate and carbonate which has been boiled for some time, saturated with carbon dioxide to form bicarbonate, and kept in a tube plugged with cotton-wool, darkens normally, although oxidase-producing organisms are likely to have been destroyed or greatly reduced in number by this treatment.

The darkening is not very sensitive to illumination. No obvious difference in rate was detected between solutions kept (*a*) in the dark and (*b*) in diffused daylight, although both Grill and Liberalli (*locc. cit.*) record an acceleration by light. The rate of oxidation rises with temperature, and with increase in the ratio of exposed area to volume. The actual volume of oxygen absorbed is by no means negligible, for in one experiment 70 c.c. of the "standard" solution at atmospheric temperature and pressure absorbed 5·5 c.c. of oxygen in 3 months.




*Retardation of the Darkening.*—Retardation of the development of colour was achieved by Greenish and Beesley (*loc. cit.*), using sulphites, bisulphites, and thiosulphates as retarders, by Liberalli (*loc. cit.*), using reducing agents (not specified in the abstract, which alone was available), by Martins (*loc. cit.*), using iodides, potassium cyanide, copper sulphate, and formaldehyde, and by Beukema-Goudsmit (*loc. cit.*), who first boiled the water with calcium carbonate. The effect of sodium thiosulphate was confirmed by Rossi (*Rev. farm., Buenos Aires*, 1933, **75**, 303).

About 40 other substances were examined as possible retarders, with only one positive result. Most of the best-known anti-oxygens were useless. Polyhydroxyphenols such as quinol and pyrogallol caused immediate coloration, and alcohols, sugars, glycerol, sulphur, acetamide, hexamine, phenol, and urea were ineffective. Thiourea, on the other hand, had marked anti-oxygenic action, even when present in very low concentration.

Most of the substances mentioned as retarders are obviously unsuitable for inclusion in medicine, and sodium thiosulphate and thiourea, both being of low toxicity (U.S.P.; Nicolas and Lebduska, *Compt. rend.*, 1928, **186**, 1441), seem to be the only two which might find practical application.

With the "standard" salicylate solution, the greatest retardation was obtained with the following concentrations: potassium iodide 1%, thiourea 0·04%, sodium thiosulphate 0·1%. With 1% iodide as retarder the colour is of the same brown shade as in the absence of a retarder, but develops about 50 times more slowly. With thiourea and sodium thiosulphate the colours are greener and yellower respectively, the reaction presumably following a different path.

The figure shows light-absorption curves obtained with a Lange photoelectric colorimeter. The curves show that the colour develops much more slowly in presence of thiourea or thiosulphate. The diminution in light absorption in the latter case after about 30 days is due to precipitation of the coloured compound. Thiourea, to the eye, appears a much better retarder than the curve would suggest, since the reading of the colorimeter is dependent on the nature, as well as on the depth, of the colour of the solution. A commonly prescribed mixture (80 grains each of sodium bicarbonate and salicylate to 8 oz. of distilled water) becomes dark brown and forms a considerable precipitate in a fortnight,

while the same solution protected by thiourea (0·04%) or sodium thiosulphate (0·1%) is still almost colourless.

*Some Points of Interest.*—It has been established that in many cases of retarded oxidation, the inhibitor is itself oxidised in the act of retardation. This is notably so in many cases where a chain mechanism exists, the products of oxidation of the inhibitor being apparently unable to propagate the reaction chain. For example, Bäckström and Alyea (*Trans. Faraday Soc.*, 1928, **24**, 601; *J. Amer. Chem. Soc.*, 1929, **51**, 90) showed that when the oxidation of sodium sulphite was retarded by *iso*propyl, butyl, or benzyl alcohol, the retarder was oxidised to the corresponding aldehyde or ketone. Again, Wagner and Brier (*Ind. Eng. Chem.*, 1931, **23**, 40) showed that the period of induction produced in the oxidation of linseed oil is proportional to the amount of quinol added, and that at the end of the induction period the reaction proceeds as if no retarder had been present. At this point, presumably, oxidation of the retarder is complete. These are only two out of many examples which might be cited.

A search was made for evidence of oxidation of sodium iodide used as a retarder, but neither free iodine nor iodate could be detected, even after some weeks. A similar experiment with sodium thiosulphate did not yield very conclnsive results, since the iodine titre of a mixture of sodium thiosulphate and bicarbonate increases with time, probably owing to formation of sulphide and trithionate (a change which takes place rapidly on heating; cf. Bassett and Durrant, J., 1927, 1418). The alteration in iodine titre was practically unaffected by sodium salicylate, which suggests that oxidation of the thiosulphate, or its decomposition products, incidental to its action as a retarder, did not take place to any great extent.

Another aspect of the problem deserves mention. A solution of sodium salicylate to which no alkali has been added does not suffer auto-oxidation, whereas the ordinary medicinal solution, containing bicarbonate, oxidises rapidly. Greenish and Beesley (*loc. cit.*) observed that replacement of the bicarbonate by sesquicarbonate (*i.e.*, by equimolar concentrations of carbonate and bicarbonate) resulted in much more rapid darkening. That the sesquicarbonate is peculiarly efficient in promoting darkening is now confirmed. As it seemed likely that this was so because the $p_H$ of the sesquicarbonate–salicylate solution happened to be particularly good for the oxidation concerned, an attempt was made to test this point.

The $p_H$ of a solution containing sodium salicylate (5%), carbonate (1·25%), and bicarbonate (1·25%) is about 10·3. A number of solutions was prepared containing salicylate (5%), bicarbonate (2·5%), and various amounts of sodium hydroxide, to give $p_H$ values from 9 to 13. Darkening was most rapid with 0·70% of the hydroxide, which gave a solution of $p_H$ close to 10·3. This result seems to strengthen belief in the importance of $p_H$. It is not, however, the only factor concerned, for little or no darkening was obtained with salicylate solutions containing (*a*) sodium hydrogen phosphate, sodium hydrogen phthalate, sodium acetate, or other salt, in place of sodium bicarbonate, and (*b*) sufficient sodium hydroxide to raise the $p_H$ to 10·3. The present work, therefore, does not contradict the suggestion of Beukema-Goudsmit (*loc. cit.*) that the bicarbonate radical plays a specific part in the oxidation, but this aspect of the matter would repay further investigation.

TRINITY COLLEGE, DUBLIN. [*Received, February 22nd*, 1938.]

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## **113.** *The* cis-*Form of Azobenzene and the Velocity of the Thermal* cis ⟶ trans-*Conversion of Azobenzene and Some Derivatives.*

By G. SPENCER HARTLEY.

Ordinary (*trans*-) azobenzene is partly converted into the *cis*-form on exposure of solutions to light. The pure *cis*-form has been isolated, and its configuration established. Its solutions absorb more light in the blue end of the visible spectrum than those of the *trans*-form, and use is made of this property to determine the concentrations in solution. In the crystalline state the *cis*-form can be kept indefinitely in the dark,

but is converted completely into the *trans*-form in solution. The conversion is a unimolecular reaction, not greatly dependent on the solvent, and the temperature coefficient corresponds to an energy of activation of 23 kg.-cals. per g.-mol.

Solutions of several derivatives of azobenzene become darker on exposure to light. This is proved in some cases, and assumed in the others, to be due to partial conversion into the *cis*-forms. The subsequent thermal *cis* ⟶ *trans*-conversion of the 4-amino-, 4-dimethylamino-, and 4-hydroxy-azobenzenes is more rapid than that of azobenzene. In the first two it is very sensitive to acid, and in the last to base, catalysis, behaviour which is attributed to very much greater ease of conversion of the ionised compounds. The conversion of azobenzene itself is catalysed by strong acids in aqueous solution but simultaneous chemical reactions occur in this case.

*The* cis-*Form of Azobenzene.*—The isolation of a second form of azobenzene from solutions exposed to light has already been reported (*Nature*, 1937, **140**, 281). Further facts indicating that this is the missing geometrical isomer, to be expected by analogy with the diazotates, diazocyanides, and azoxy-compounds, have since been established. The evidence may be summarised as follows:

(1) That the new form is converted completely into the ordinary form on heating in a small enclosed space without change of pressure is evidence of the identity in chemical composition of the two forms. (2) Freezing-point determinations on 5% solutions in benzene and acetic acid gave depressions of 1·44° and 1·09° respectively, corresponding to $M = 179$ and 190 (Calc. for $C_{12}H_{10}N_2$ : $M$, 182), and thus disposing of the remote possibility of the new form being a polymer. (3) The new form has a dipole moment of 3·0 D. in benzene solution, according to measurements by R. J. W. Le Fèvre, whereas that of the normal form is zero (*idem*; and Bergmann *et al.*, *Ber.*, 1930, **63**, 2572). (4) The new form, though differing by only 3° in m. p., is considerably more soluble in polar solvents, particularly in water ($6·5 \times 10^{-4}$ mol./l. at 25° as compared with $2 \times 10^{-5}$), and less soluble in petrol (b. p. 40—60°) at 0° (*ca.* 0·9%; cf. 3·5% for ordinary form). (5) The preparative agent (light) is one which is known to be particularly active in promoting geometrical rearrangement about a double bond, *e.g.*, in fumaric-maleic acids (Warburg, *Ber. Berl. Akad.*, 1919, 960), stilbene (Smakula, *Z. physikal. Chem.*, 1934, *B*, **25**, 90), oximes (Brady and McHugh, J., 1924, **125**, 547), azoxybenzene (Müller, *Annalen*, 1932, **493**, 166), and diazocyanides (present paper).

It may therefore be taken as established that the new form is the *cis*-isomer, the ordinary form being *trans*, as shown by its zero moment (see above) and its crystal structure (Robertson *et al.*, *Proc. Roy. Soc.*, 1936, *A*, **154**, 197, and private communication).

In the crystalline state the *cis*-form appears to be quite stable in the dark at room temperature. It forms small, bright red crystals from petrol. The m. p., determined by quick plunging, is 71·4°; it falls on repeated measurement, owing to rapid conversion in the liquid state at this temperature into the *trans*-form. The course of the m. p.'s on slow repetition was a simple fall to a eutectic at 41°, followed by a rise to that of the pure *trans*-form at 68·0°.

Dilute solutions of the same concentration of either form quickly become identical on exposure to daylight. The equilibrium mixture contains 15—40% of the *cis*-form, depending on the solvent. This concentration is determined, at ordinary temperatures and light intensities, entirely by the relative velocities of the two photochemical reactions, *cis* ⟶ *trans* and *trans* ⟶ *cis*. The thermal reaction occurs only in the *cis* ⟶ *trans* direction, but is too slow to have any influence on the photochemical equilibrium. In the remainder of this paper we are concerned mainly with the thermal reaction. The photochemical reaction is being further investigated in these laboratories.

An approximate measurement of the heat evolved in the *cis* ⟶ *trans* reaction was made by melting weighed quantities of the two forms on mercury at about 135° in a small Dewar vessel. At this temperature the *cis* ⟶ *trans* reaction is almost instantaneous. The heats absorbed per g. were: for the process, solid *trans* at 21° ⟶ liquid *trans* at 135°, 84, 77, and 79 cals. (3 expts.), and for solid *cis* at 21° ⟶ liquid *trans* at 135°, 15 and 16 cals. (2 expts.). For the process, solid *cis* at 21° ⟶ solid *trans* at 21°, we obtain, therefore, the surprisingly large value of 65 cals. evolved per g. (12 kg.-cals./g.-mol.).

cis–trans-*Isomerism in Derivatives.*—It was to be expected that other azo-compounds would pass partly into the *cis*-form on exposure of solutions to light. It was found that 4 : 4′-dimethylazobenzene behaved similarly to azobenzene in that the light absorption increased on exposure of an acetone solution and the solute became in part more resistant to precipitation by water. Isolation of the *cis*-form was not attempted. 4-Methoxyazobenzene showed the same behaviour; isolation was attempted by the same method as for *cis*-azobenzene (see p. 637), but the chloroform extract left behind a viscous red oil which failed to crystallise at − 15°. A dilute solution of the dried oil had a greater light absorption than that of a solution of the same weight concentration of the normal crystalline substance. After exposure of the solutions to light the absorption readings were identical and intermediate between those of the original solutions.

Samples of *cis*- and *trans*-*p*-bromobenzenediazocyanides, kindly supplied by Mr. H. Vine, were made up in identical concentration in benzene. The former had the greater absorption. After exposure to daylight both reached the same intermediate absorption, found, by calibration with mixtures, to correspond to 20% of the *cis*-form.

The question arose whether the important class of azo-dyes might show the same behaviour. Almost all these substances have hydroxy-, amino-, or substituted amino-groups in the *o*- or the *p*-position to the azo-group. For this reason the behaviour of some 4-amino- and 4-hydroxy-derivatives in various solvents was examined. 2-Substituted isomers would be expected to behave, at least qualitatively, in the same way. The compounds examined were 4-hydroxy-, 4-amino-, 4-dimethylamino-, and 4-methoxyazobenzenes, and the fully methylated quaternary ammonium salt. All showed appreciable darkening in some solvents on exposure to light, reverting to normal at different rates in the dark. With the first three compounds, the thermal reversion to the stable form was much too rapid in hydroxylic solvents to permit the method of isolation used for azobenzene to be applied. The quaternary salt reverts very slowly, but in this case isolation of the *cis*-form would have required a closer study of the solubilities of the salts with various anions than the object in view seemed to justify. That the change in absorption on exposure is, in these compounds also, due to the photochemical production of the *cis*-form is therefore at present an assumption based on analogy.

*Method of Analysis.*—A photometric method was used to determine the amounts of *cis*- and *trans*-forms of azobenzene in a given solution, since the former has a greater absorbing power for blue light than the latter (between 2 and 3 times as great, depending on solvent). A photoelectric null instrument of a new type, to be described elsewhere, enabled a reading on the sliding scale of a neutral-tinted glass wedge compensator to be obtained for solutions within a certain concentration range (*ca.* 3—8 × $10^{-4}$ mol./l.) in a Hilger Pyrex cell 2 cm. long. The light used was that from a high-temperature tungsten lamp, passed through a Kodak Wratten filter, No. 47 (transmission band approx. 4000—4800 A). The intensity was insufficient to effect appreciable photochemical change during a measurement. It was assumed in the work previously reported that the scale reading was linear against percentage composition, since it was found to be linear against concentration for the pure *trans*-compound. This assumption was found to be not strictly true. Calibration curves were therefore constructed for acetone as solvent. Experiments in other solvents were carried out at much higher concentrations, so that no effect of solvent on the photometer reading remained after dilution with acetone to the concentration convenient for analysis.

Solutions of known total concentration were diluted quantitatively with acetone, and the percentage of the *cis*-form could then be obtained from the photometer reading by interpolation on the family of calibration curves with an accuracy of 0·5—1·0% (Method 1).

Solutions of the concentration convenient for analysis have, for a given concentration, photometer readings independent of the initial isomeric composition, if they have been exposed to bright daylight (not necessarily sunlight) for a few minutes. This enabled the concentrations of both forms to be determined in cases where quantitative dilution was not convenient. Dilution was continued till a convenient photometer reading was obtained, the diluted solution exposed, and a second reading obtained. The total concentration corresponding to the latter was found from one curve, and the percentage composition of the original solution then obtained from the family as before. This method (Method 2) was necessarily rather less accurate (about 1·0—1·5%). The fully exposed dilute solutions in acetone contained 25% of the *cis*-form,

the higher value of 27% previously reported being due to the inaccurate assumption mentioned above.

In the case of the azobenzene derivatives, the absorption, in the narrow blue region used, was not always increased on exposure. In the dimethylamino-compound, considerable reduction resulted, especially in acetone, but the visual colour increased considerably. The visible band must therefore be considerably displaced, not, as in azobenzene itself, being increased in intensity without displacement (Le Fèvre and Vine, this vol., p. 438).

*Conversion Velocity Measurements.*—All operations except the illuminations were carried out in a darkened room lit by a carbon-filament 32 c.p. lamp, which was found to cause no appreciable change in a cold *cis*-azobenzene solution in ½ hour. To prevent photochemical change when the room was more brightly lit for other work, the water of the 25° thermostat tank in which the reaction vessels were placed was stained with methyl-orange, and the solid and the *trans*-solutions were kept in a dark cupboard.

The velocity of the dark reaction in azobenzene was followed in solutions of concentration $8{\cdot}0 \times 10^{-3}$ mol./l., 1 c.c. being taken at intervals and diluted to 25 c.c. with acetone for analysis. With acetone itself, further measurements were made at the analytical concentration. In experiments at 25°, Method 1 was used. At higher temperatures it was desired to withdraw samples quickly and to run them into cold acetone to stop the reaction. The pipetting was therefore done only approximately, and Method 2 applied. For the pure liquid, samples were withdrawn by dipping in a glass rod and washing it with acetone, Method 2 again being used in the analysis. The constant higher temperatures were obtained by jacketting the reaction vessels with vapour of boiling acetone, carbon tetrachloride or water. The reaction vessels, of about 10 c.c. capacity, had ground glass stoppers and necks; the latter extended beyond the ground part, so that the vapour jacket could extend above the stopper.

In making measurements in water a different procedure was necessitated by the fact that the solubility of the *trans*-form is much below the concentration convenient for accurate photometric measurements. The reactions were therefore carried out in shaken vessels, and solid *trans*-azobenzene was added. The *trans*-form has a negligible tendency to form a supersaturated solution and is removed from the solutions as it is formed. Samples were withdrawn through a micro-filter (Jena glass) and the concentration of the remaining *cis*-form determined photometrically. These measurements were made at 25° only. At temperatures above the eutectic, the *cis*-form would be partly removed in a liquid phase and the method would therefore not be applicable.

The reaction in water is catalysed by hydrogen ions. Measurements were made, by the method used for water, in various concentrations of several strong acids.

Measurements were made of the velocity of conversion in benzene solution of *cis*-*p*-bromobenzenediazocyanide by the same method as for azobenzene. The results were in good agreement with the measurements of Le Fèvre and Vine (*loc. cit.*) by the dielectric-constant method.

For the measurements on methoxyazobenzene, solutions of the *cis*-rich oil (see p. 635) were used, the photometer being calibrated by mixtures of this solution with one of equal concentration of the ordinary (*trans*-) form. For the quaternary ammonium compound in water and the dimethylamino-compound in acetone, the light-equilibrium solution was the starting material, calibration being effected by mixtures with unexposed solution of equal concentration. In the case of the former, the photometer reading displacement was small, and the results therefore less accurate. That the amount of *cis*-form is in each case unknown by a constant factor is of no consequence, of course, for the calculation of the first-order velocity constant.

The light absorption of exposed solutions of the amino- and hydroxy-compounds in all solvents and of the dimethylamino-compound in petrol and benzene reverted to the normal value in the dark too quickly for calibration of the photometer by mixtures to be possible. The difference of photometer reading from the dark value had therefore to be taken to be proportional to the amount of *cis*-form. The logarithms of these differences plotted against time gave lines which were straight within the large random error due to the difference in these cases being small (corresponding to 5—15% change in mean extinction), to the measurements being of necessity made in the photometer cell which was not thermostatically controlled, and perhaps also to changing catalytic effects. The velocity constants are therefore very crude, the accuracy being perhaps only 10—25%, but they differ so greatly that the figures are nevertheless of considerable significance.

The hydroxy-, amino-, and dimethylamino-compounds were very sensitive to base or acid catalysis. In alcoholic solution no changes of absorption could be detected on exposure,

except slight ones in the last compound. It is unlikely that the absorption curves of *cis*- and *trans*-forms will be identical, and the use of a different light filter again gave no change. The most obvious explanation is that the thermal reaction is too quick to permit the photochemical reaction to be detected. The same applied to the dimethylamino- and the amino-compound in acetone until a trace (*ca.* $10^{-5}$N) of piperidine was added to neutralise the acidity due to atmospheric carbon dioxide. A change on exposure was then found, disappearing in the dark at a rate corresponding to a half-life period of no less than 6 hours for the *cis*-form of the first-named. Addition of piperidine to the benzene and the petrol solutions of these compounds enabled more reproducible conversion rates to be obtained. The apparently analogous addition of benzoic acid to the benzene solution of the hydroxy-compound accelerated the reaction. Measurements were made of the conversion velocities of the amino- and the dimethylamino-compound in acetone (with piperidine) with addition of acetic acid and methyl alcohol in increasing concentration. The additions were made quickly *after* exposure of the alkaline solutions. The catalytic influence of acid on the dimethylamino-compound in acetone can readily be demonstrated. If two test-tubes are filled with the same dilute solution (with a trace of piperidine) and one is exposed to sunlight for a few minutes, the latter is obviously more deeply coloured. If now a few drops of acetic acid are added to the first, no change is apparent, but if it is added to the second, the colour is seen to return to normal in a few seconds.

The catalytic effects of piperidine, methyl alcohol, and benzoic acid on the conversion of the exposed solntions of the hydroxy-compound in benzene were similarly examined.

The results are recorded in Table I.

*Preparations.*—trans-*Azobenzene.* The commercial product is nearly pure *trans*. Only one sample examined contained a detectable amount (less than 2%) of *cis*. Pure *trans*-form was prepared by two methods, *viz.*, (i) recrystallisation of the commercial product from an alcoholic solution boiled for 6 hours in the dark, and (ii) successive partial precipitation by water from acetone solution. M. p.'s and photometer readings were in exact agreement.

trans-4-*Hydroxy-, -4-amino-, and -4-dimethylamino-azobenzenes.* The first was prepared by coupling diazotised aniline with phenol, and the others were commercial products. All were purified by several recrystallisations from water–alcohol and petrol–benzene.

trans-4-*Methoxyazobenzene.* The purified hydroxy-compound was methylated, the product extracted by benzene from alkaline aqueous alcohol, and recrystallised from methyl alcohol.

trans-*Azobenzene-4-trimethylammonium nitrate.* The purified 4-dimethylamino-compound was condensed with methyl sulphate in nitrobenzene at 150°, the cooled solution decanted from tarry by-products, and the methosulphate extracted with water. The extract was made alkaline with sodium carbonate and non-ionised products extracted with benzene; the quaternary nitrate was then precipitated with ammonium nitrate. It recrystallised very well from water.

cis-*Azobenzene.* Experiments showed that even from heavy petrol, in which the ratio of the solubilities of the *cis*- to the *trans*-form would be expected to be a minimum, the latter is the first to crystallise out after exposure to light. A larger preparation of the *cis*-form was therefore carried out by a modification of the method previously described. A saturated solution (*ca.* 10%) of ordinary azobenzene in 500 c.c. of glacial acetic acid (to which 10 c.c. of water were added to stop freezing) was placed in a large, white, enamelled-iron tray with a glass cover in bright light on the roof. Acetic acid was preferred to acetone or alcohol on account of its smaller volatility and of its affording a higher percentage of *cis*-form. After 3—4 hours, the proportion of *cis*-form (determined by Method 2) reached a steady value of 24%. The solution was then diluted in the dark with 450 c.c. of water (an amount found by experiment to precipitate nearly all the *trans* and none of the *cis*) and filtered. The residue was used for further exposures. The filtrate was diluted with a further 500 c.c. of water and extracted with chloroform. The extract was washed with water and evaporated in a vacuum at once, the crude product being then dried, the main essential for an efficient yield being to get the *cis* form in the solid state as soon as possible. The crude products of several exposures were united and crystallised from petrol between room temperature and that of an ice–salt freezing mixture. Crystallisation was stopped as soon as a fraction having an appreciable content of *trans* (Method 2) came out. Purification was carried out by recrystallisation, care being taken to wash each batch of crystals with cold petrol to remove mother-liquor, which always contains a little *trans*-form due to thermal conversion. Identity of m. p.'s and of photometer readings of standard solutions of successive fractions was used as a criterion of purity. The yield of pure *cis*-form was 8 g. per exposure (of 50 g.).

TABLE I.

*Thermal* cis ⟶ trans-*conversion in azobenzenes.*

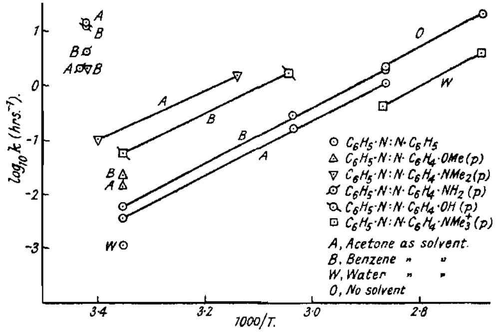
| Solvent. | Temp. | Half-life period. | Solvent. | Temp. | Half-life period. |
|---|---|---|---|---|---|
| *(a)* 4-Hydroxyazobenzene. | | | | | |
| Petrol (b. p. 40—60°) | 19° | 3·0 mins. | $C_6H_6$ + 0·4% MeOH | 19° | 0·5 mins. |
| $C_6H_6$ | ,, | 3·3 ,, | ,, 5 × $10^{-6}$N-$C_5H_{11}N$ | 21 | 1·6 ,, |
| ,, + 0·5% $Ph{\cdot}CO_2H$ | ,, | 1·2 ,, | ,, 10 ,, ,, ,, | ,, | 1·0 ,, |
| ,, + 0·1% MeOH | ,, | 2·1 ,, | $COMe_2$ | 19 | 2·9 ,, |
| ,, + 0·25% ,, | ,, | 0·9 ,, | | | |
| *(b)* 4-Aminoazobenzene. | | | | | |
| Petrol + 3 × $10^{-3}$N-$C_5H_{11}N$ | | | | 19 | 9 ,, |
| $C_6H_6$ + ,, ,, | | | | ,, | 10 ,, |
| $COMe_2$ + ,, ,, | | | | 18 | 20 ,, |
| ,, + ,, ,, + 2% MeOH | | | | ,, | 3·8 ,, |
| ,, + ,, ,, + 4% ,, | | | | ,, | 2·5 ,, |
| ,, + ,, ,, + 6% ,, | | | | ,, | 1·8 ,, |
| ,, + ,, ,, + 6 × $10^{-3}$N-HOAc | | | | 21 | 0·4 ,, |
| *(c)* 4-Dimethylaminoazobenzene. | | | | | |
| Petrol + 3 × $10^{-3}$N-$C_5H_{11}N$ | | | | 19 | 5·0 ,, |
| $C_6H_6$ + ,, ,, | | | | ,, | 21 ,, |
| $COMe_2$ + ,, ,, | | | | ,, | 360 ,, |
| ,, + 5 ,, ,, | | | | 21 | 390 ,, |
| ,, + ,, ,, | | | | 45·5 | 26 ,, |
| ,, + ,, ,, + 8% MeOH | | | | 20 | 200 ,, |
| ,, + ,, ,, + 7·4 × $10^{-3}$N-HOAc | | | | 18 | 70 ,, |
| ,, + ,, ,, + 13·8 ,, ,, | | | | ,, | 21 ,, |
| ,, + ,, ,, + 27·3 ,, ,, | | | | ,, | 6·7 ,, |
| ,, + ,, ,, + 38·4 ,, ,, | | | | ,, | 4·0 ,, |
| ,, + ,, ,, + 49·4 ,, ,, | | | | ,, | 2·6 ,, |
| ,, + 2·5 ,, + 25·3 ,, ,, | | | | ,, | 4·8 ,, |
| *(d)* 4-Methoxyazobenzene. | | | | | |
| $C_6H_6$ | 25 | 30 hrs. | 50% $COMe_2$–$H_2O$ | 25 | 63 hrs. |
| $COMe_2$ | ,, | 49 ,, | | | |
| *(e)* Azobenzene-4-trimethylammonium ion. | | | | | |
| $H_2O$ | 75·6 | 1·6 ,, | $H_2O$ | 99·5 | 0·16 ,, |
| *(f)* Azobenzene. | | | | | |
| Pure liquid | 76·6 | 19 mins. | $COMe_2$ | 25 | 198 hrs. |
| ,, | 100 | 1·8 ,, | $H_2O$ | ,, | 600 ,, |
| $CCl_4$ | 25 | 94 hrs. | ,, + 1·0N-NaOH | ,, | 860 ,, |
| ,, | 56·4 | 2·3 ,, | ,, + 1·0N-NaCl | ,, | 600 ,, |
| ,, | 76·6 | 0·29 ,, | ,, + 0·26N-HCl | ,, | 73 ,, |
| $C_6H_6$ | 25 | 119 ,, | ,, + 0·56 ,, | ,, | 35 ,, |
| ,, | 56·4 | 2·5 ,, | ,, + 0·96 ,, | ,, | 16 ,, |
| ,, | 76·6 | 0·35 ,, | ,, + 4·16 ,, | ,, | (*ca.* 0·7 ,, ) |
| HOAc | 25 | 186 ,, | ,, + 0·23N-$HClO_4$ | ,, | 79 ,, |
| ,, | 56·4 | 4·2 ,, | ,, + 0·53 ,, | ,, | 30 ,, |
| ,, | 76·6 | 0·60 ,, | ,, + 0·26N-$H_2SO_4$ | ,, | 98 ,, |
| ,, + 50% water | 25 | 360 ,, | ,, + 0·54 ,, | ,, | 61 ,, |

## RESULTS AND DISCUSSION.

The conversion followed the first-order equation in all cases. The results of all the measurements are recorded in Table I as half-life periods. In Fig. 1, the logarithms (decadic) of the velocity constants (in hours$^{-1}$) for the non-catalytic conversion are plotted against reciprocal absolute temperature. For azobenzene itself, in two solvents at three temperatures and in the fused state at two, the points lie, as nearly as can be expected for measurements in condensed systems, on parallel straight lines. The slopes give a mean activation energy of 23 kg.-cals./g.-mol. For the diazocyanide we find 22 (Le Fèvre and Vine give 21·5) and for dimethylaminoazobenzene 21 kg.-cals. This slight decrease with increasing ease of conversion of the compound does not require a different mechanism for the reaction in different substances. Although the velocity increases over 10,000-fold

from azobenzene and the quaternary salt in water to hydroxyazobenzene in petrol, there is no clear separation into "fast" and "slow" groups. Moreover, the general influence of solvent, when acid or base catalysis does not occur, is the same whatever the substituent, the velocity decreasing with increasing polarity and polarisability of the solvent. The only apparent exception to this is of doubtful significance—the *cis*-hydroxy-compound is converted appreciably more quickly in acetone than in benzene, but this is probably explained by the very great sensitivity of this compound to the hydroxyl group, which will be present in small amount in the enolic form of the ketone, and by absorption of atmospheric moisture.

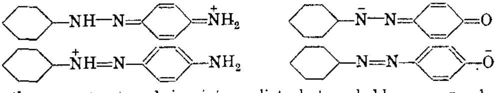
FIG. 1.




*Influence of temperature and of substituents on the non-catalysed conversion.*

The classical explanation of the change in absorption spectra on ionisation of amino- or hydroxy-azo-compounds was that the ions had the quinonoid structures (I), in support of which there was the production of compounds identical with the above when synthesis of the phenylhydrazones of benzoquinoneimide or benzoquinone was attempted. We should now say that the relationship between (I) and the azo-structures (II) is that of

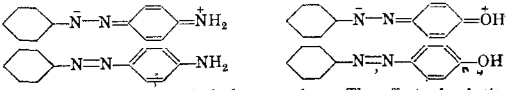
(I.) (II.)




mesomerism, the true structure being intermediate but probably more nearly (I) than (II). The weakness of the N=N double bond in the ion provides an explanation of the acid or base catalysis of the *cis* ⟶ *trans* conversion. Rotation about the N–N axis in the ion will be almost free, and the double bond will therefore re-form to give the stable (*trans*) configuration, when the ion loses or gains a proton to re-form the uncharged molecule.

The uncharged molecule may be considered to be mesomeric between the corresponding structures (III) and (IV), but will be much more nearly (IV) than (III), since the non-

(III.) (IV.)




catalysed *cis* ⟶ *trans* reaction is relatively very slow. The effect of substituents on the non-catalysed reaction increases roughly with increase of electron release from the

4-substituent, as would be expected for the mechanism proposed, the electron-repelling substituents favouring the quinonoid form. The retarding effect of polar non-hydroxylic solvents is probably best regarded as due to reduction of the repulsion between the -C-N= dipoles. In hydroxylic solvents, a chain of molecules with hydrogen bonds from the amino- or the hydroxyl group to the remoter azo-nitrogen atom could, as it were, close the external circuit and permit resonance between (III) and (IV) without ionisation

Whether or not this last mechanism is operative in pure hydroxylic solvents we have not at present the experimental evidence to decide, but the catalysis by methyl alcohol in dilute solution (see Figs. 2, 3, and 4) requires that there should also be a *uni*molecular reaction with hydroxylic molecules. Most probably the hydroxyl group functions as a base or acid, and is naturally much weaker in these properties than piperidine and acetic acid respectively.

*Acid and base catalysis.*

Fig. 2.

*4-Dimethylaminoazobenzene in acetone (corrected to 18°).*

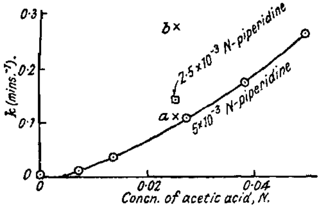
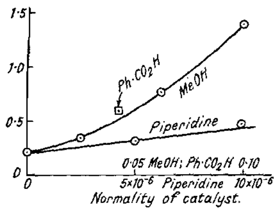



Fig. 4.

*4-Hydroxyazobenzene in benzene (corrected to 19°).*



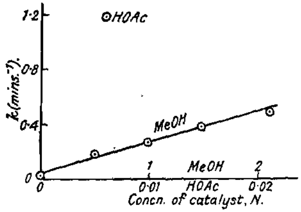




Fig. 3.

*4-Aminoazobenzene in acetone (with* $3 \times 10^{-3}$N-*piperidine) (corrected to* 18°).

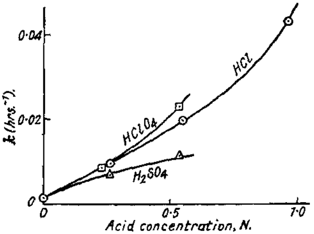


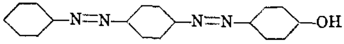

Fig. 5.

*Azobenzene in aqueous acids at* 25°.

It will be seen from Figs. 2 and 3 that the amino- is much more sensitive to acid catalysis than the dimethylamino-compound. The actual concentration of ionised form is in both cases extremely small, as is evident from the fact that a strong acid must be added to acetone solutions before the characteristic pink colour appears. The full curve in Fig. 2 refers to measurements with one concentration of piperidine, and the point ⊡ to half this concentration. The points × give the velocities from the curve, corresponding to (*a*) the same excess concentration of acetic acid over piperidine as obtains at ⊡, and (*b*) the same ratio of excess acetic acid to piperidine, which ratio will determine the "hydrogen ion" ($[HO{\cdot}CMe_2]^+$) concentration in the buffer solution. That the observed velocity is intermediate, indicates that *both* hydrogen ion and undissociated acid are

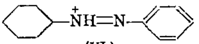
effective. The former is much the more effective, since, when no base is present to produce the buffer action, the much weaker acid, carbon dioxide, is sufficient to promote a very rapid reaction. When base is present, however, the concentration of hydrogen ions will be very low.

The extreme sensitivity of the amino- and the hydroxy-compounds to acid or basic substances makes it at once evident that the *cis*-form will never be produced in appreciable amounts in the ordinary azo-dyes, made and applied as they are in aqueous media. Even when a second diazotisation and coupling have been effected, as in analogues of (V), the

(V.) 

same mechanism can operate right through to the more remote azo-group, so that this also, though less affected, would probably be far too easily reconverted into the *trans*-form thermally to permit the photochemical reaction to build up an appreciable amount of the *cis*-form in aqueous media.

The acid catalysis of the reaction in azobenzene itself is presumably due to the azo-nitrogen atoms functioning as bases. It is well known that azobenzene behaves as a base, although a very weak one, being somewhat soluble in concentrated mineral acids. The positive charge on the nitrogen atom in the normal form of the ion (VI) will facilitate electron transfer from an *o*- or *p*-carbon atom (VII). The mechanism is therefore the same as in the acid catalysis of the amino-derivatives but of an altogether different order of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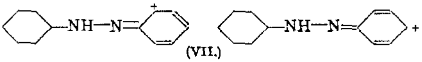
(VII.)

magnitude, requiring a considerable concentration of mineral acid to produce an appreciable effect. It was necessary, in the measurement of the reaction in acid and salt solutions, to measure the solubility of the *trans*-form therein. These measurements were extended to the *cis*-form (the solution in this case being saturated with both forms at once, and the photometer reading corrected for the small concentration of *trans*-form present). The results (Table II) give some idea of the concentration of the azobenzene ions. In

TABLE II.

*Solubility of azobenzene in acid, alkali, and salt solutions (g.-mols./l.).*

| Solvent. | *trans*-. | *cis*-. | Solvent. | *trans*-. | *cis*-. |
|---|---|---|---|---|---|
| Water | $2·4 \times 10^{-5}$ | $6·45 \times 10^{-4}$ | ½N-HCl | $2·3 \times 10^{-5}$ | $6·28 \times 10^{-4}$ |
| ½N-NaCl | 1·65 „ | 4·64 „ | N-HCl | 2·15 „ | 6·40 „ |
| N-NaCl | 1·2 „ | 3·68 „ | N-NaOH | 1·3 „ | — |

these relatively low acid concentrations it appears that the formation of ions only just counteracts the ordinary "salting-out" effect. If the hydrochloric acid has the same salting-out effect as sodium chloride, we should conclude that, in N-acid, about half of the azobenzene exists as a cation. The *cis*-form is not much, if at all, more basic than the *trans*. The conversion velocity of the ions must therefore be about 100 times greater than that of the neutral molecules.

*Decomposition in Acid Solutions.*—The measurements in acid solutions indicated that some side reaction accompanies the *cis* ⟶ *trans*-conversion, because the photometer readings approached asymptotically considerably higher values than for the saturated solutions of pure *trans*-form. The half-life times recorded are calculated from the first part of the log (apparent concentration)–time curves. That, in the N/2- and N/4-acid at least, we are measuring approximately the rate of *cis* ⟶ *trans*-conversion, seems certain. The velocities (Fig. 5) are proportional to the acid concentrations for hydrochloric and perchloric acids, and are smaller for sulphuric acid, as is to be expected from the incomplete second dissociation of the last. The amount of side product, on the other hand, judged by the discrepancy between extrapolated and expected "infinity" readings, is dependent on the nature of the acid. The apparent velocity of conversion in 4N-hydrochloric acid is much more than 4 times that in

1N. A second-order reaction is therefore appearing. This is apparently still mainly a *cis* ⟶ *trans*-reaction, for, although the solid product obtained in this case was certainly not pure *trans*-azobenzene, a considerable yield of substance melting sharply at 68° was obtained by recrystallising it from methyl alcohol. A good yield was obtained by the same method from *cis*-azobenzene dissolved in 4N-perchloric acid and kept for 2 hours. Second-order catalysis presumably requires that the second nitrogen atom can also accept a proton.

There may also occur a decomposition of the type investigated by Jacobson (*Annalen*, 1909, **367**, 304) when hydrogen chloride was passed into a solution of azobenzene in methyl alcohol, and benzidine, chloroanilines, and chlorosemidines were produced with evolution of chlorine. *cis*-Azobenzene causes evolution of chlorine from *aqueous* hydrochloric acid. So does the *trans*-form, but in less degree, probably owing to its smaller solubility. At least one product is formed on treatment of *cis*-azobenzene with concentrated acid which is not produced from the *trans*-form. The solutions are red and remain red, even on heating, and, on dilution and repeated extraction with benzene, a pink compound remains in the aqueous layer. It is strongly adsorbed at the benzene interface, is precipitated in a yellow form on addition of alkali, is then soluble in benzene and can be recovered in the pink form by aqueous acid, behaviour characteristic of an aminoazo-compound of rather high molecular weight. It is formed in 10N-solutions of hydrochloric, perchloric, sulphuric, or nitric acid, in increasing amount in the order given, but is not produced at all from *trans*-azobenzene, even on exposure to sunlight.

I am greatly indebted to Profs. C. K. Ingold and S. Sugden, and to Drs. C. F. Goodeve, A. Wassermann, C. L. Wilson, and R. J. W. Le Fèvre for their valuable interest and advice, and to the last-named in addition for measurement of the dipole moment of *cis*-azobenzene.

The Sir William Ramsay and Ralph Forster Laboratories,
University College, London. [*Received, February 28th,* 1938.]

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## **114.** *Studies in the Growth of Metal Trees in Gels. Part I. The Morphology of the Lead Tree.*

By Alexander King and Norman Stuart.

The growth of lead trees by displacement of lead from solution by less noble metals has been studied in the presence of silica gel. Detailed experiments, tin being used as the reducing metal, indicate that the morphology of the lead tree produced is fundamentally dependent on the concentration of lead in the gel, a wide variety of growth types being obtained. One of these is a new, spiriform type of growth which is characteristic of lead concentrations of 0·02N.

Lead trees produced by metals far removed from lead in the electrochemical series are similar in form among themselves, but different from that of the lead trees grown from tin; no spiriform growths are produced in this case.

Colloidal materials in the gel have an inhibiting or modifying influence on the structure of the lead trees, which is unpredictable.

More than 100 years ago, Fischer (*Pogg. Ann.*, 1827, **10**, 603) observed that if a zinc rod was suspended in a solution containing 1 part of lead salt, 1½ parts of acetic acid, and 100 parts of water, a vegetable-like growth of metallic lead gradually sprouted from the zinc. This structure he termed the *arbor saturni*, and the corresponding tree of metallic tin was called the *arbor jovi*. Similar results were obtained by substituting iron, cadmium, or manganese for zinc in the above experiment. That magnesium would function in place of zinc was noticed by Roussin (*Chem. News*, 1866, **14**, 27) and Bryant (*ibid.*, 1899, **79**, 75), who reported the evolution of hydrogen during reduction by magnesium. Cossa (*Bull. Soc. chim.*, 1870, **14**, 199) studied the reduction of lead salts by aluminium.

Although it had previously been reported that tin would not displace lead from solutions of its salts, Sackur (*Z. Elektrochem.*, 1904, **10**, 523) made the important observation that lead is completely precipitated by tin from its solution in acetic acid, whereas tin is precipitated by lead from solutions of its salts in nitric acid. In hydrochloric and sulphuric acids

an equilibrium is set up between tin, lead, and the salts of the two metals. The precipitation of lead by tin from lead perchlorate solution acidified by perchloric acid was studied by Noyes and Taube (*J. Amer. Chem. Soc.*, 1917, **39**, 1532) when measuring the electrode potential of lead.

Wöhler (*Annalen*, 1853, **85**, 253) discovered that if water is poured on a concentrated solution of lead nitrate or acetate so as to form a separate layer, and a piece of lead added so that it is dipping into both liquids, small crystals of lead were formed on that part of the metal immersed in the more concentrated solution. Senderens (*Bull. Soc. chim.*, 1894, **11**, 424) obtained similar results by the interaction of lead with neutral lead nitrate solution in the absence of air.

Lead may also be produced in an arboreal form by electrolysis of its salts. Lehmann (*Z. Krist.*, 1890, **17**, 277) considered that the electrolytic formation of metal crystals was very similar to normal crystallisation from solution. He noticed that although a low current density produced a uniform deposit of metal, a higher density resulted in the formation of a skeleton-like structure of metal, further increase in cnrrent strength altering only the mass of the crystals but not their form. Lead was rather exceptional in this connexion, for, with a weak current, leafy crystals apparently belonging to the monoclinic system and very similar in appearance to those of the chemically produced lead tree were formed, whereas with stronger currents crystals belonging to the cubic system, and under the best conditions, well-formed octahedra, were deposited. He assumed that these were due to the separation of a different molecular species of lead in solution, followed by subsequent crystallisation. Cohen and Inouye (*Chem. Weekblad*, 1910, **7**, 454) showed, by means of *E.M.F.* measurements that the supposed cubic and monoclinic forms were identical and thus not allotropic. Further work on the form of electrodeposited lead was carried out by Elbs and Rixon (*Z. Elektrochem.*, 1903, **9**, 267), who stated that lead separates sometimes as large shining plates and at other times as a sponge, the latter condition being due to the presence of plumbic salts in solution; and by Kohlschütter and Übersax (*ibid.*, 1924, **30**, 72), who measured the velocity of growth of deposited lead with varying current density. At low current densities, massive, leafy crystals were formed, at higher densities " crystal chains," the velocity of growth of which increased as the lead-ion concentration decreased.

The fact that trees of similar form can be grown by chemical means or by electrolytic deposition makes it clear that the mechanism of formation of the lead tree is essentially electrochemical, and this is borne out by a study of lead equilibrium between metallic lead and lead nitrate solution which results in the growth of a tree. Von Hevesy (*Physikal. Z.*, 1915, **16**, 52) measured this equilibrium by the use of thorium-*B* as an indicator, and concluded that the rate of exchange of lead between the solid metal and the solution was too great to be due to thermodynamic equilibrium but was caused rather by the action of local electric currents, lead passing into solution at some points and being precipitated at others. The electrochemical nature of the process is also stressed by Kohlschütter (Festschr. Tschirch, Bern, 1926, p. 425), who formulates the reduction of lead salts by zinc thus: $Pb^{++} + Zn \rightleftharpoons Pb + Zn^{++}$. He ascribes the outward form of the tree to local concentration differences, as well as to the position of nuclei and to the crystal system to which the tree-forming metal belongs. The growth is also influenced by concentration cells set up owing to the formation of adsorbed, semipermeable films of basic salts of lead.

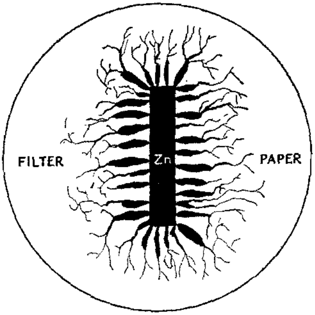
The characteristic feature of the ordinary lead tree, which becomes apparent to the eye when growth has been prolonged for a considerable time, is the extraordinary flatness of the leaflets, growth apparently taking place in two dimensions only and chiefly in one. A clue to the reason for this is given by Evans (*Chem. and Ind.*, 1925, **44**, 791, 812), who argues that the latent heat of crystallisation is dissipated by convection currents, etc., more easily at edges and at corners than in the centre of flat faces. This naturally causes growth to be quicker and more extensive at edges, and leads to the growth of platelets. Evans then gives directions for the formation of a two-dimensional lead tree. These are so important as to demand full description here. A filter-paper saturated with 10% lead acetate solution is placed on a sheet of glass, and a strip of zinc, the lower edge of which has been freshly cut, placed on top of the wet paper. In a few hours a two-dimensional tree grows out,

having the form shown diagrammatically in Fig. 1. The obvious fact of metal dissolution at some points and deposition at others at once establishes the process as electrochemical, the current passing along the slender fronds of deposited metal and returning through the wet filter-paper—a fairly high resistance circuit. If the resistance of the circuit is reduced by the addition of sodium acetate to the lead acetate solution with which the filter-paper is impregnated, the velocity of growth becomes much faster owing to greater conductivity.

The question as to why the lead is deposited so far from the zinc is answered by dipping the filter-paper containing the tree into dilute ammonium sulphide solution, whereupon a deep brown coloration indicates the presence and position of lead ions. This coloration is seen to occupy the whole paper except near the tree, a very faint colour being noticed between the fronds in the outer zone but none in the inner zone. Hence, after the process has been proceeding for some time, no deposition of lead can take place on the zinc, as there are no lead ions in the neighbourhood. The outgrowths, however, can still continue to extend, as they are in constant contact with the outer, unexhausted reservoir of lead ions.

The essential difference in appearance between the two-dimensional lead tree grown on a filter-paper and that normally prepared in solution is the development of structure and branching of the fine fronds in the former case. This is presumably due to the fact that an ordinary tree in solution is in close proximity to the zinc, this inner region of growth never becoming completely free from lead ions which are continually being replenished by convection currents, etc. It must be stated, however, that a definite two-dimensional platelet structure accompanied by branching often does become apparent in the tree as ordinarily grown, although to a minor degree.

Fig. 1.




From what has just been said it follows that the best means of studying the growth and morphology of metal trees is to produce them in a gel, where convection, mechanical disturbances, etc., are absent and electrolyte movement can only take place by diffusion or by electrolytic migration. It is to be expected that, under gel conditions, growth would extend for much longer distances from the reducing metal and produce a morphology characteristic of the conditions employed.

Simon (*Kolloid-Z.*, 1913, 12, 171) carried out the reduction of lead salts by zinc in the presence of silica gel: to a 15% sodium silicate solution he added a slight excess of 50% acetic acid and about 10% of concentrated lead acetate solution, the mixture then being allowed to gel in test tubes. A piece of zinc was then inserted in the gel at the top of each tube; and in a few days trees had grown and extended throughout the length of the tube. The two photographic reproductions in Simon's paper show that the trees consisted of branched metal strips.

Just as it now appears that the Liesegang phenomenon in gels represents the normal course of precipitation when convection and mechanical disturbances are eliminated, the function of the gel being a secondary consideration, so will metal trees grown in gels probably represent perfect growth which is only suggested but never attained in ordinary solution.

In the present work many trees have been grown in silica gel, and the influence of lead-ion concentration, acidity, position of the reducing metal in the electrochemical series, gel rigidity, etc., on the morphology of growth determined.

## Experimental

In all experiments, except those on the effect of gel rigidity, a standard gel was used, which was prepared by mixing a given volume of 2N-acetic acid with twice its volume of sodium

silicate solution of $d$ 1·06 and an equal volume of water in which the required quantity of lead salt was dissolved. The time of gelation varied widely according to the amount of electrolyte present, but was generally of the order of a few hours. If this order of mixing of the ingredients of the gel system was adhered to, precipitation of the lead was avoided, although those gels which contained a high concentration of lead salts were somewhat turbid.

In all the experiments described in this paper, the gel was contained in boiling tubes measuring 3·5 × 15 cm. A number of preliminary results have shown that the shape of the vessel has, as might be expected, a considerable influence on the form of the lead tree. This effect is being fully investigated.

Reduction was started by inserting a piece of metal into the gel at the top of each tube so that it was almost submerged. In a number of cases, especially those in which gelation did not take place till after a considerable time, the metal was suspended in the fluid mixture by means of a thread. Preliminary investigation seemed to indicate that different forms of growth were obtained according to whether the metal was suspended in the liquid system before gelation or inserted into the corresponding gel. A large number of mixtures of silicate, lead acetate, and acetic acid were therefore made in duplicate, the reducing metal being placed in the system (*a*) before and (*b*) after gelation. Although the conditions were chosen so as to produce a wide range of growth types, the differences between the (*a*) and (*b*) series were in no instance fundamental.

Most of the results to be described were obtained by the reduction of lead acetate in silica gel by metallic tin. The tin was usually inserted in the granulated form, although at times it was found more convenient to use thin sticks of cast tin, prepared by pouring the molten metal into a hard-glass tube and afterwards etching the surface. Comparative experiments showed that there was no difference in the type of growth produced in a given gel by the two types of metal.

*Results.*

(a) *The Influence of Lead Concentration.*—A series of gels were prepared, containing different amounts of lead acetate, with respect to which they varied from 0·1 to 0·001N. Reduction was effected in each case by means of tin, and the following results obtained.

*Series I.* (1) 0·1N-Gel. Very long, two-dimensional, sword-like growths of bright metal were obtained, which were characteristically straight and had little branching tendency. The width of the sword was of the order of 0·5 cm. Peculiar double growths appeared at the top of the tube [see Plate I (*a*)].

(2) 0·08N-Gel. Growth was very similar to the above. The sword-like growths, which were slightly and irregularly serrated, extended the whole length of the tube and there were more side branches [Plate I (*b*)].

(3) 0·06N-Gel. The tree, although still flat, was not so obviously uniplanar as those formed at higher lead concentrations. It was strikingly branched, all the branches being inclined at the same angle to the main " stem." Furthermore, secondary branches grew from the primary branches and were parallel to the main " stem," thus giving a peculiar lattice effect.

(4) 0·04N-Gel. The growths, although still fairly flat, were much less broad and less regularly branched. The existence of a main " stem " was less obvious, there being numerous " stems " of about the same magnitude growing from the tin inserted at the top of the gel. The plane of the growths had a tendency to twist slightly but regularly. The growth was more copious than at higher lead concentrations [see Plate I (*c*)].

(5) 0·025N-Gel. The whole structure of the metal was much finer, the growth being very copious, and the tendency of the flat ribbons of metal to twist more marked.

(6) 0·02N-Gel. The tree was still finer than with 0·025N-lead and was strikingly spiriform, somewhat resembling a very deeply cut screw having a minute barrel diameter and a very serrated edge to the pitch. The small branches, which were very frequent and regular, were all inclined at the same angle to the main " stems " and thus helped to emphasise the spiriform nature of the growth [Plate I (*d*)].

(7) 0·015N-Gel. The growth was again finer; the filaments were less straight and seemed to twist irregularly. Spiriform structure was still observed but was much less obvious for two reasons, *viz.*, because the pitch was much greater and because the side branches grew off the main filaments at different angles. The total amount of growth was noticeably less in this specimen than in those at higher lead concentrations, and its rate slower.

(8) 0·0125N-Gel. The growth was finer than that of (7) but very similar in structure [see Plate I (*e*)].

(9) 0·01N-Gel. The filaments were now very fine and branched. They appeared on close

examination to be spiriform, but the thinness of the filaments made this very difficult to see. The total amount of growth was small.

(10) 0·0075N-Gel. A very few, hair-like filaments grew slowly from the tin but only penetrated a few cm. into the gel [see Plate I (*f*)].

(11) 0·001N-Gel. No growth.

The above series of experiments was several times repeated, the reproducibility of the forms described being established. It thus appears that the form of the lead tree is fundamentally dependent on the concentration of lead in the solution. Abundant additional evidence of this fact is presented below, it being found that, even when the other conditions are varied considerably, the form of growth produced by reduction is invariably that characteristic of the lead concentration.

Three main types of lead tree appear to be formed: at high lead concentrations, flat, straight, sword-like growths; at concentrations in the neighbourhood of 0·02N-lead acetate, strikingly spiriform growths; and at still lower concentrations, fine, irregular, branched filaments. Of these three types, the spiral growth is the most noteworthy, and it had not been described until one of us published a preliminary note on this structure (Stuart, *Nature*, 1937, **140**, 589). Arising electrochemically, these spiriform crystals are entirely different from those helical and spiral precipitates of lead iodide, lead chromate, and calcium phosphate described by Hatschek and his collaborators (*Kolloid-Z.*, 1920, **27**, 225; *Biochem. J.*, 1920, **14**, 418), nor do they resemble the spiral crystals of Copisarow (*Kolloid-Z.*, 1929, **47**, 60).

In the above series of experiments it was found that growth was most easily induced in gels with low lead concentration; indeed, in the higher lead content gels, it was frequently necessary to wash the tin in dilute hydrochloric acid before inserting it in the gel, in order to induce growth. The total amount of growth, as well as its rate, appeared to be maximum at medium lead concentrations (0·06—0·04N) and to decrease gradually to zero in either direction.

(*b*) *The Influence of Acid Concentration in the Gel.*—A series of gels were now prepared in which only the quantity of acetic acid was varied. The results are collected in Table I, the normality of the acid representing the total quantity added and not the amount of free acid remaining after neutralisation of the silicate. The normality of the gel with respect to lead acetate was 0·02 in each case, *i.e.*, corresponding to the system producing the spiral growth. Reduction was affected by means of tin.

TABLE I.

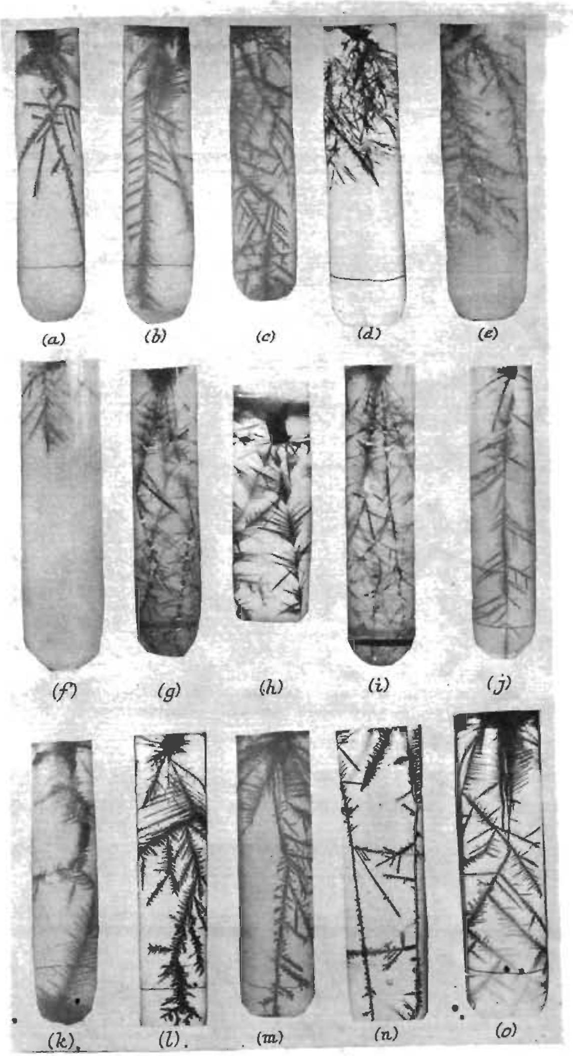
*Series II.*

| No. | Acid concn., N. | Time of gelation. | Description of tree. |
|---|---|---|---|
| 1 | 0·25 | 20 mins. | No growth. |
| 2 | 0·3125 | 5 mins. | No growth but a greyish membrane on the tin surface. |
| 3 | 0·375 | 15 mins. | Short growth of rather flat, branched type. |
| 4 | 0·4375 | 1 hr. | Rather irregular fine growths; much branched; spirals of large pitch. |
| 5 | 0·5 * | 3 hrs. | Distinct spirals of rather large pitch which opens out lower in the tube. |
| 6 | 0·55 | 3 hrs. | Larger spirals, but of smaller pitch than those of (5). The pitch opens out lower in the tube and finally gives place to a fine, irregular, branched growth. |
| 7 | 0·6 | 6 hrs. | Spirals still larger and more developed than in (6): see Plate I (*g*). |
| 8 | 0·7 | 12 hrs. | Very similar to 7: see Plate I (*h*). |
| 9 | 0·8 | 18 hrs. | Pitch of spirals is much smaller and opens out lower down in the tube: see Plate I (*i*). |
| 10 | 0·9 | 24 hrs. | Very similar to 9. |
| 11 | 1·0 | 24 hrs. | Spiral of different type, resembling a thin ribbon of lead twisted into a spiriform strip. The edge of the ribbon was unserrated and there were practically no small branches. The few branches which were formed were long and of similar form to the main stem. See Plate I (*j*). |

* Identical in conditions and form with Series I, No. 6.

In view of the fact that variation in the amount of acid had only a secondary effect on the spiriform growths characteristic of 0·02N-lead acetate, similar experiments were carried out with 0·08N- and 0·0125N-lead gels, the results being recorded in Table II, (*a*) and (*b*), respectively.

Several general tendencies emerge from these results; first, and most important, acid concentration has, except at the extreme ends of the scale, little effect on the form of growth, which is essentially conditioned by the lead concentration. Thus the trees of Series II are essentially spiriform, the acid concentration producing only secondary variations. Series III and IV are typical of 0·08N- and 0·0125N-lead concentrations respectively.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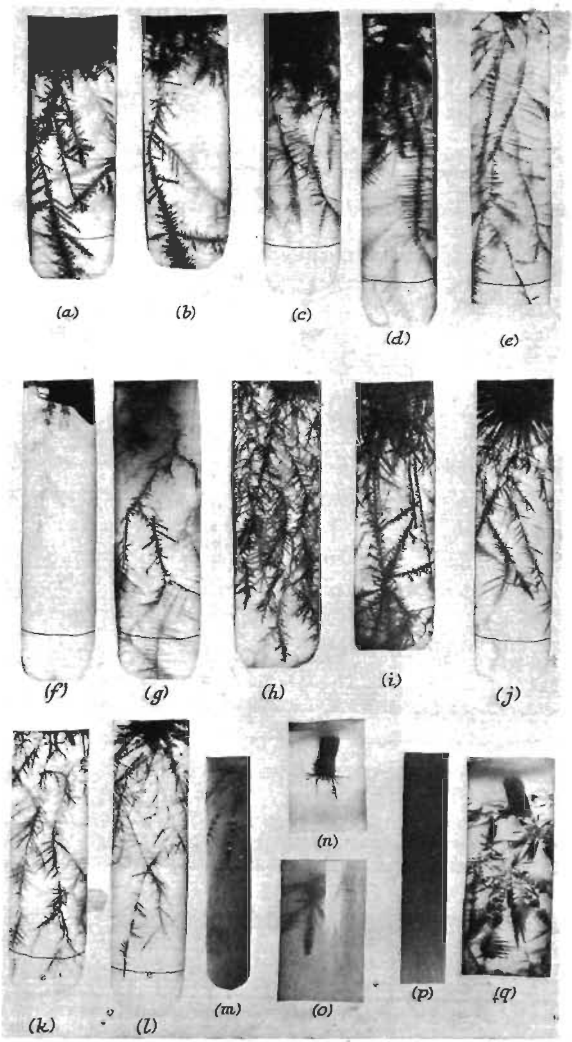
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TABLE II.

(*a*) *Series III. Lead acetate* = 0·08N. *Acetic acid concentration varied.*

| No. | Acid concn., N. | Description of tree. |
|---|---|---|
| 1 | 0·375 | A grey skin formed on the tin within a few days and, in the course of months, very broad two-dimensional platelets of length *ca.* 1 cm. grew. |
| 2 * | 0·5 | Long, flat, sword-like growths. |
| 3 | 0·625 | Very flat, jagged, sword-like growths with a few side branches all emerging at the same angle to the main stem. |
| 4 | 0·75 | Long, flat growths similar to the above but even wider. |
| 5 | 1·0 | Much less growth than at lower concentrations but still strikingly flat. |
| 6 | 1·5 | Grey membrane of lead on the tin. |

* Identical in conditions and form with Series I, No. 2.

(*b*) *Series IV. Lead acetate* = 0·0125N. *Acid concentration varied.*

| No. | Acid concn., N. | Description of tree. |
|---|---|---|
| 1 | 0·375 | Very small, very fine, branched tree. |
| 2 | 0·5 † | Irregular, twisted, fine growth; much twisting; some spiral tendency. |
| 3 | 0·625 | Similar to (2) but much coarser and with the spiral tendency more evident. Total amount of growth is maximum for the series. The filaments become noticeably coarser at the bottom of the tube. |
| 4 | 0·75 | Very similar to (3) but considerably less growth. Spiriform tendency is still slight. |
| 5 | 1·0 | Very slow and small growth which finally produces a single straight filament with numerous parallel side branches at right angles to it. |
| 6 | 1·5 | No growth or deposit on the tin. |

† Identical in conditions and form with Series I, No. 8.

It also appears that there is an upper limit of acid concentration above which growth will not take place (*ca.* 1·5N) and a lower one below which it is negligibly slow. In the middle range of acid concentration, growth reaches its maximum in both rate and amount.

Further general tendencies are observed in the spiriform growths of Series II (that of the optimum concentration of this growth type). The spirals are of small pitch at the top of the tube and consist of spiriform strips whose small, regular, side branches all emerge at the same angle and make the spiriform nature of the structure strikingly obvious. As the growth descends in the tube, the spiral pitch increases gradually and at the same time branching becomes more irregular, the side branches emerging at different angles to the main stem. The spiriform feature thus becomes much less prominent and resembles the type of structure normally produced at slightly lower lead concentrations. The growth at the lowest part of the tube is very irregular and, consisting as it does, of fine branched filaments, resembles the growth at *ca.* 0·0125N-lead.

The silica gel prepared by the neutralisation of sodium silicate by acetic acid contains a high concentration of sodium acetate which should probably form an efficient buffer for acetic acid. As this seemed a possible explanation of the unexpected lack of influence of the action of acid on the morphology of the lead trees, a series of $p_H$ determinations was carried out with gels prepared from various amounts of acid. The results are collected below:

*The $p_H$ values of gels of various acid contents.*

| | | | | | | |
|---|---|---|---|---|---|---|
| Normality of gel with respect to total vol. of added acid | 0 | 0·125 | 0·25 | 0·3 | 0·35 | 0·4 |
| $p_H$ | 10·0 * | 10·0 | 10·0 | 10·0 | 9·5 | 4·3 |
| Normality of gel with respect to total vol. of added acid | 0·5 | 0·6 | 0·7 | 0·8 | 0·9 | 1·0 |
| $p_H$ | 4·0 | 4·0 | 4·0 | 4·0 | 4·0 | 4·0 |

* Precipitate of lead hydroxide.

They show that, between concentrations of 0·4 and 1·0N, the acid is effectively buffered. This was the concentration range at which growth was found to take place, only the 0·35N-specimens being of abnormal form. The secondary modifications in growth form as well as of rate and magnitude of growth are thus to be ascribed to the acetate-ion concentration.

In view of the failure of the above experiments to produce systems of varying hydrogen-ion concentration, a series of gels was prepared from sodium silicate and nitric acid to which lead nitrate had been added. The acidity was adjusted so that 8 gels of constant lead nitrate concentration but with different $p_H$ values between 3·5 and 8·5 were formed. On the addition of tin, reduction did not take place, nor was the metal in the least corroded. It is thus established that although tin will displace lead from solutions of some of its salts (in gels) it will not do so from other salts. Further work on this point is in progress. (See also Table X.)

(c) *Trees produced at Higher Lead Concentrations.*—In Series I it was found impossible to work at higher than 0·1N-lead acetate concentrations owing to precipitation. The effect of acid concentration having been investigated, a series of gels was prepared in which the acetic acid was increased from 0·5 to 1·25N, and the lead acetate concentration varied. The results, collected in Table III, are observations of the trees after 3 months' growth.

TABLE III.

*Series V. Acetic acid concentration* 1·25N. *Lead acetate concentration varied.*

| No. | Pb, N. | Description of tree. |
|---|---|---|
| 1 | 0·25 | No growth. |
| 2 | 0·2 | Minute growths on some parts of the metal. |
| 3 | 0·17 | Granular membrane covering the tin. |
| 4 | 0·135 | Very coarse growth; not flat: see Plate I (*k*). |
| 5 | 0·10 | Copious growth of the lattice type (cf. Series I, No. 3). The structure is very fine at the top of the tube, but coarser below. |
| 6 | 0·085 | *The most copious growth observed in the course of the present work;* very flat, coarse, and extremely irregular tree of the lattice type: see Plate I (*l*). |

(d) *The Influence of Gel Rigidity.*—Although it appears from the study of periodic precipitation in gels that the phenomenon is essentially due to the elimination of mechanical and convectional disturbances, yet it is true that the gel may exert a fundamental and often specific effect. For instance, although it is possible to prepare Liesegang rings of silver chromate in gelatin, lead chromate rings cannot be formed, although just the opposite holds good in agar gels. All the present work has been carried out in silica gel which, because of its lack of protective properties, would be expected to have less influence than any other gel on the crystal form and rate of growth. It is hoped soon to extend the work to other gels. The present series of experiments concerns the effect of gel rigidity on the form of the lead trees. As the concentration of acetate has been shown to have a secondary modifying effect (see above), an excess of sodium acetate was added in the case of the more dilute gels so that the acetate concentration should be constant throughout the series. The figures in col. 2 of Table IV represent the fraction or multiple of the silica concentration of the standard gel (see p. 644) in the specimen under investigation. The excess of free acid present after neutralisation of the silicate was adjusted in each case to 6·5 c.c. of 2N-solution per 80 c.c. of gel, this being the same as in the standard gel.

The physical effect of gelation appears to have considerable effect on the electrochemical behaviour of the system, because, in the sol, reduction of lead acetate by the tin cannot take place whereas immediately after gelation (without any chemical change) reduction commences. In all but the most liquid gels (which appear to produce trees of irregular morphology) the lead tree is once again typical of the lead concentration employed, *e.g.*, those of Series VI were of the spiriform type, those of Series VII of the sword type. In the former instance, increasing rigidity of the gel had the effect of compressing the spirals, thus decreasing the pitch and at the same time producing narrower strips of metal. In practically every case it is noticed that the main direction of growth of the lead tree is parallel to the axis of the tube, even when the tube is allowed to rest in a horizontal position during growth. In Series VI, No. 3, growth was made to take place simultaneously from both ends of the gel and was of the same type and magnitude in each case, gravity obviously having little effect.

(e) *Rate of Growth.*—In order to give some idea of the rate of growth of the lead tree, a large test tube (36 × 4·5 cm.) was filled with a silica gel made 0·08N with respect to lead acetate, and growth induced, as usual, by tin. The tree produced was of the sword type characteristic of this lead concentration, and grew at the rate of 1·5 cm. per diem for the first 6 days, after which it grew much less rapidly and was 15·2 cm. long at the end of 3 weeks; the rate of growth was then 0·25 cm. per diem. By the end of 2 months the tree was 24·8 cm. long, and a further 5·1 cm. were added during the third month. It should be noted that growth is much faster at slightly lower lead concentrations but, being less straight, is difficult to measure.

The marked diminution of growth as the tree extends well down into the tube is due, not only to the decrease in the concentration of lead ions, but also to the extended length of the electrochemical circuit between the growing tip of lead and the tin.

(f) *Reduction by Other Metals.*—Many of the features of the morphology of lead trees produced by reduction of lead salts by tin may be due to the fact that these two metals are adjacent in the electrochemical series and have normal electrode potentials which are exceptionally close.

TABLE IV.

(*a*) *Series VI. Lead acetate* 0·2N. *Silicate concentration varied.*

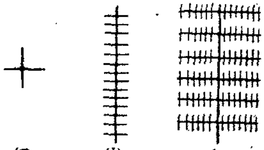
| No. | Gel rigidity. | Time of gelation. | Description of tree. |
|---|---|---|---|
| 1 | 0·125 | 6 days | The tin was suspended in the liquid 1 day after mixing. During the next 5 days no growth or change in appearance of the tin took place. Immediately after gelation to a very liquid gel, growth began, and after 28 days reached 1/3 of the length of the tube. Thereafter no further growth. The tree was rather coarse at the top and very irregular, there being no sign of spiriform structure; the lower part of the growth was very irregular and angular. |
| 2 | 0·25 | 2 days | The tin was again suspended in the sol but did not effect reduction. Immediately on gelation, growth of the lead tree commenced and proceeded until the bottom of the tube was reached. The upper part of the growth consisted of very bright and broad spiriform strips, the pitch opening lower down, as in Series II. At the bottom of the tube were fine, irregular annular strips as in (1). |
| 3 | 0·5 | 24 hrs. | Tin was inserted at the bottom of the tube before gelation and at the top afterwards. The growths from both ends were identical and strikingly spiriform, the pitch opening progressively from the metal. The two trees met in the middle of the tube without overlapping, both being fine and much branched in this region. |
| 4 | 0·75 | 24 hrs. | Spiriform growth, much finer than (2) or (3), with opening pitch and increased branching lower in the tube. |
| 5 | 1·0 | 4 hrs. | Fine, spiriform tree, smilar to (4) but with smaller total amount of growth. |
| 6 | 1·25 | 0·5 hr. | Spiriform structure, noticeably finer and tighter than (5). Pitch of spiral *ca.* 2·5 mm. After 28 days, growth had reached only half-way down the tube, and after a further month had not increased. |
| 7 | 1·375 | 15 mins. | Spiriform growth even finer than (6), so that the spirals are difficult to see with the naked eye. Considerable amount of branching, but as in (6) the branches are unserrated metal strips. |

(*b*) *Series VII. Lead acetate* 0·08N. *Silicate concentration varied.*

| | | |
|---|---|---|
| 1 | 0·125 | Does not gel: no growth even after 2 months. |
| 2 | 0·25 | Very liquid gel in which spongy mass of metal, *ca.* 3 cm. long, is formed. |
| 3 | 0·5 | Very transparent gel: very thin, two-dimensional branched sword-like growths very similar to those of Series I, No. 1, appear. Total length of growth 7·5 cm. Granular spots noticeable on the shiny metal surface. |
| 4 | 0·75 | Very copious tree of the Series I, No. 1, type; near the top are large serrated fan-like structures: see Plate I (*m*). |
| 5 | 1·0 | Tree growth not so copious, but the " swords " are longer and straighter than in (3) or (4): see Plate I (*n*). |
| 6 | 1·25 | Very copious growth with huge fan-like structures above, and heavy branched swords below: see Plate I (*o*). |

For this reason it is to be expected that external conditions might have a relatively large effect on electrochemical behaviour and hence tree growth than for any other two metals in the series. That being so, reduction by other less noble metals should produce a morphology different from those already described and be less susceptible to changes in concentration, etc. A series of lead trees were therefore grown by reduction by means of zinc in gels containing different concentrations of lead acetate. These experiments are described in Table V, which corresponds exactly to the tin reductions of Series I. A new type of growth is observed in this series, *viz.*, the cross type depicted diagrammatically in Fig. 2.

FIG. 2.



(*a*) *End on* (*b*) *Side view* (*c*) *Branched type*

The trees produced by zinc reduction are essentially different from those by tin, in the initial, almost instantaneous production of a black spongy mass of metal from which flat, irregular growths of the sword type slowly develop, and in the cross type of growth which is characteristic of medium and low lead concentrations. Once again the effect of lead concentration is all important, and it is significant that the sword type of growth found to be characteristic of high lead-concentration, tin-induced trees is also produced by zinc reduction at the same concentration. Once again, rate and magnitude of growth are maximum in the region of 0·06N-lead acetate gels. Spiriform growth was not observed.

TABLE V.

*Series VIII. Acid concentration* 0·5N. *Lead concentration varied. Reducing metal, zinc.*

| No. | [Pb]. | Description of tree. |
|---|---|---|
| 1 | 0·125 | Within 10 seconds the zinc is covered with a black velvet skin of lead which grows outwards to form a spongy mass of thickness *ca.* 1 cm. By the end of 24 hrs., coarse, flat, serrated fronds of bright silver colour have begun to grow from the sponge and these slowly increase in size for a few weeks, by which time they are very similar to the sword type of Series I, No. 1, but more irregular: see Plate II (*a*). |
| 2 | 0·1 | Very similar to (1) but growth less coarse. The main growth is essentially of the latticed sword type, but after one month, fine filaments of the cross type appear at the bottom of the tube. |
| 3 | 0·05 | The sponge-like growth at the top of the tube is now clearly seen to be composed of fine, entangled filaments of the cross type. The later, slower growth is still of the sword type but is less obviously flat and more branched. Cross filaments grow from the sword tips in later stages: see Plate II (*b*). |
| 4 | 0·04 | The sponge-like growth is now much less black and the slower growth from it now consists of parallel filaments the branches of which are short (Fig. 2, *a*, *b*). One flat sword growth appears in the midst of the latter. |
| 5 | 0·02 | Much less growth than above. The metal is now of a pale grey colour: see Plate II (*c*). |
| 6 | 0·015 | Pale grey cross filaments with much branching of the type of Fig. 2, *c*. |
| 7 | 0·01 | There was now no spongy growth round the zinc, the cross fronds growing directly from the metal. These are fewer and finer than before but with longer primary and secondary branches: see Plate II (*d*). |
| 8 | 0·0075 | A few pale grey filaments of extremely fine structure and with long branches reach to the bottom of the tube: see Plate II (*e*). |
| 9 | 0·002 | Almost invisibly fine, hair-like growth from the metal, extending only a few cm. into the gel: see Plate II (*f*). |
| 10 | 0·001 | No visible growth. |

TABLE VI.

*Series IX. Acid concentration* 0·5N. *Lead acetate concentration varied. Reducing metal, aluminium.*

| No. | [Pb]. | Description of tree. |
|---|---|---|
| 1 | 0·125 | Very flat, branched growths similar to the sword type of tin but more irregular. |
| 2 | 0·1 | Much as (1), but more copious growth and rather more regular. At the bottom of the tube the fronds become very fine. |
| 3 | 0·08 | Coarse, flat growths with much irregular branching. |
| 4 | 0·04 | Less growth than (3) and finer. A few filaments of the cross type appear below. |
| 5 | 0·03 | The cross type of growth now predominates in the upper part of the tube but there are still numerous unbranched, flat fronds. |
| 6 | 0·02 | Very similar to (5), but the fronds are now very fine and less obviously flat: see Plate II (*g*). |
| 7 | 0·01 | Fewer, longer, finer cross growths similar to the zinc-induced tree of Series VIII, No. 7, but ending in fine, irregular branched growths very similar to those of the tin tree of this concentration. |
| 8 | 0·0075 | Exceedingly fine, pale grey tree of the cross type, very similar in form to, but smaller than, the zinc-reduced tree at the same lead concentration. |

The aluminium used for reduction had to be washed in acid before introduction into the gel. Growth of the lead tree started immediately, producing a spongy growth which appeared to be complete within a few hours. The later structures grew slowly down from this and appeared to be stationary after about 4 weeks. In general the lead trees reduced by aluminium resembled those by zinc, but the flat growths at high lead concentrations were rather more irregular and less like those of the tin-reduced trees. At medium lead concentrations the cross type of structure predominated, and at still lower concentrations tended to end in fine, branched growths. The results are recorded in Table VI.

The formation of the trees with magnesium (Table VII) was somewhat different from the others. Immediately on introduction of the metal an evolution of hydrogen commenced; this produced large lenticular bubbles in the gel, which somewhat obscured the growth. In some cases these appeared several inches below the growing tip of the tree. At higher lead concentrations a black lead sponge grew quickly from the magnesium. The lead trees were very small in this series and growth was complete in about a day. The structure was of the cross filament type throughout, there being no trace of the "sword" and other types produced by reduction with other metals. Oxidation of the magnesium produced a white precipitate in

TABLE VII.

*Series X. Acid concentration* 0·5N. *Lead acetate concentration varied. Reducing metal, magnesium.*

| No. | [Pb]. | Description of tree. |
|---|---|---|
| 1 | 0·125 | Immediate production of a lead sponge round the magnesium; from this a few irregular platelets appeared within a day and had grown no more by the end of 2 months. |
| 2 | 0·08 | More growth than in (1) and rather less irregular. A few cross filaments appeared. Growth complete in one day. |
| 3 | 0·06 | Rather irregular tree of the cross filament type was complete in 1 day. Total amount of growth small. |
| 4 | 0·03 | Similar to (3) but cross filaments very distinct. |
| 5 | 0·01 | Very fine, branched cross growth similar to the corresponding trees reduced by zinc or aluminium. |
| 6 | 0·0075 | Growth almost obscured by bubbles; very fine and of pale colour. |

the upper part of the tube, which tended to spread downward, especially along the strands of metal, which became coated with small white crystals eventually giving the structure the appearance of snow-covered trees.

The metals zinc, aluminium, and magnesium are somewhat removed from lead in the electrochemical series and produce trees of a morphology resembling one another, but lacking in the structural detail and regularity of the trees produced by tin. In no case could any trace of spiral structure be observed. The more noble metals adjacent in the series to tin are cobalt and nickel, but even when etched with acid or used in the form of a fine powder, they would not replace lead from lead acetate solution in silica gel. A series of reductions was carried out by means of iron and cadmium, the next metals in the series. The results of these experiments are collected in Table VIII.

TABLE VIII.

(*a*) *Series XI. Acid concentration* 0·5N. *Lead acetate concentration varied. Reducing metal, iron.*

| No. | [Pb]. | Description of tree. |
|---|---|---|
| 1 | 0·125 | Long, straight, unbranched sword-like growth, irregularly serrated. |
| 2 | 0·08 | Long, irregular branched swords, the whole structure becoming progressively coarser with distance from the iron. |
| 3 | 0·04 | Much finer than (2) and more branched. |
| 4 | 0·03 | Still finer than (3); long, twisting fronds with many branches extend to the bottom of the tube. In the upper part of the tube are many spiriform growths which are extremely fine and of very small pitch: see Plate II (*h*). |
| 5 | 0·02 | Much less growth than in (4), and tree obscured by bubbles and iron oxidation products. |
| 6 | 0·015 | Structure is predominantly of the cross type, but a few minute, tight spirals can be seen. |
| 7 | 0·01 | Rather fine tree of the cross type. |
| 8 | 0·0075 | As (7) but finer. |

(*b*) *Series XII. Acid concentration* 0·5N. *Lead concentration varied. Reducing metal, cadmium.*

| | | |
|---|---|---|
| 1 | 0·125 | A close mass of grey, unbranched spines *ca.* 3 cm. long grows out from the metal. Below this, long, irregularly branched swords extend to the bottom of the tube: see Plate II (*i*). |
| 2 | 0·08 | The spines surrounding the metal have now small, regular branches; the main, sword-like growth is straight and more branched. |
| 3 | 0·06 | The spines surrounding the cadmium are now clearly of the cross filament type, rather coarse and very straight. Growth in the lower part of the tube is finer than before. |
| 4 | 0·04 | Still less and finer growth than in (3). The cross filaments radiating from the cadmium are fewer and quite straight. |
| 5 | 0·03 | Growth now extends only half-way down the tube and is less regular and flat. The cross filaments surrounding the cadmium are fewer and larger. One or two minute spirals of small pitch were noted: see Plate II (*j*). |
| 6 | 0·02 | The structure is now mostly of the cross type and extends almost to the bottom of the tube, changing to the fine branched type in the lowest part. Spiriform growth is more obvious than in (5): see Plate II (*k*). |
| 7 | 0·015 | Fewer and finer but longer cross growths, some of which become branched below. Spiriform tendency is still noticeable: see Plate II (*l*). |
| 8 | 0·0075 | Long, branched cross filaments of a pale grey colour; no spirals. |

The trees produced by reduction with iron and cadmium are transitional between those with tin and with the less noble metals zinc, aluminium, and magnesium. As with tin, there was no

immediate growth of a lead sponge, although a tendency in this direction was manifest in the cadmium growths which formed a close mass of straight spines round the reducing metal. At high lead concentrations sword-like growths were produced, which were similar to those from tin but less regular. In the region of 0·03—0·015N-lead concentration, spiriform structures were observed as with tin, although these were much less prominent and more difficult to see than with the latter metal.

The growths from iron, like those from magnesium, were obscured by oxidation products, a rust coloration gradually diffusing throughout the tube. In this series, the cross filament type of structure, which is predominant in trees produced by less noble metals and entirely absent in tin-reduced trees, first makes its appearance, but only at the lowest concentrations. Iron wire would not effect displacement of lead from lead acetate, even after etching with acid; iron powders, especially those produced by low-temperature reduction, were active in this connection.

The results of a few miscellaneous reductions are described in Table IX.

TABLE IX.

*Series XIII. Acid concentration* 0·5N.

| No. | Reducing metal. | [Pb]. | Description of tree. |
|---|---|---|---|
| 1 | Mn | 0·02 | Pale grey cross type of growth very similar to that produced by zinc at the same concentration. |
| 2 | Cr | 0·02 | Do. |
| 3 | Amalgamated Sn | 0·06 | No growth. |
| 4 | Pb | 0·04 * | A grey skin of metal formed round the lead. |
| 5 | Cu | 0·02 | A coherent black coating covered the etched copper wire, and the blue colour of the cupric ion appeared in the gel, gradually diffusing throughout. A fine, black veil-like deposit of lead grew out about 1 cm. from the copper in all directions. |

* Stannous acetate.

Chromium and manganese produced trees identical with one another and with those grown from zinc and aluminium at the same concentration of lead. Most surprising was the observation that the more noble metal copper displaced lead from lead acetate solution in the gel.

(g) *The Influence of Non-electrolytes and Protective Colloids on the Lead Tree.*—It has long been known that the addition of gelatin or glue to the electrolyte may modify the form of metals produced by electrodeposition in the case of lead. Freundlich and Fischer (*Z. Elektrochem.*, 1912, **18**, 885) investigated the effect of gelatin on the form of lead deposited from its acid solution by zinc, and found that smaller crystals were produced. Gray (J., 1925, **127**, 776) found that the presence of colloids tended to diminish the size of deposited lead crystals and increase their cohesive power, presumably owing to an adsorbed film of the colloid.

In some preliminary experiments, a few drops of B.D.H. universal indicator were added to the gel, with the result that the form of growth of the lead tree was considerably modified and, when larger amounts of indicator were used, completely inhibited. Several reductions were therefore carried out under various conditions, in the presence of different organic materials. These experiments, some of which have been repeated and found to be reproducible, are described in Table X.

It thus appears that colloidal materials invariably change the form of the lead tree, the results being unpredictable. The total amount of growth is usually reduced by the colloid and the branches or filaments become finer in texture and less regular. The inhibition of growth, or diminution in its rate, is presumably due to adsorption of the colloid on the growing surface of the metal and "sealing" of active centres.

## DISCUSSION.

The foregoing results, which relate the morphology of the lead tree to external conditions, are chiefly remarkable for their reproducibility and for the fact that the growth type is so sensitive to small changes in the lead concentration of the gel.

The mechanism of formation of the trees is obviously electrochemical, and many of the observations indicate that the electrochemical equilibrium must be profoundly modified by some of the changes in condition employed here. Especially unexpected was the effect of gelation on the system (Series VI, No. 1; VII, Nos. 1, 2); before gelation, tin would not

TABLE X.

*Lead acetate* 0·02N. *Different organic materials added to the gel before setting.*

| No. | Acid concn., N. | Reducing metal. | Substance added. | Description of tree. |
|---|---|---|---|---|
| 1 | 0·5 | Sn | Universal indicator | Normal spiriform growth but with hair-like side branches. At the bottom of the tube the spirals change to a wisp of hair-like filaments: see Plate II (*m*). |
| 2 | 0·65 | Sn | Do. | A serrated ribbon of bright metal, about 8 mm. wide, twisted into a spiriform strip. |
| 3 | 0·9 | Sn | Do. | Lead-coloured membrane forms round the tin and a few short, branched needles grow in the course of 3 months: see Plate II (*n*). |
| 4 | 0·65 | Zn | Do. | Instead of the normal cross filament type, grey threads of metal, so fine as to be almost invisible, spread parallel throughout the length of the tube: see Plate II (*p*). |
| 5 | 0·9 | Zn | Do. | Do. |
| 6 | 0·65 | Sn | 2·0% Alcohol | Normal growth. |
| 7 | 0·65 | Sn | 2·0% Acetone | Do. |
| 8 | 0·65 | Sn | 1% Sucrose | Spiriform growth, much coarser than normal. |
| 9 | 0·65 | Sn | 0·1% Gelatin | Spiral tree broader than usual but with a small total amount of growth. |
| 10 | 0·65 | Sn | 0·1% Soluble starch | A few sharp, straight spines grow to the length of 2 cm. in the course of 3 months: see Plate II (*o*). |
| 11 | 0·5 | Sn | 0·2% Gum arabic | No growth |
| 12 | 0·5 | Sn | 0·1% Agar | Do. |
| 13 | 0·8 | Sn | Universal indicator (3 drops) | Numerous spirals of close pitch: see Plate II (*q*). |

replace lead from solution; immediately after setting of the gel, reduction commenced. This, and the extraordinary effect of colloidal materials on the rate and amount of growth, suggest that the gel may, after all, have a specific effect on the morphology of the growth.

Generally there is a change in structure type as the tree grows down into the tube; regular spiriform growths, for example (characteristic of 0·02N-gels), generally descend with increasing pitch, develop irregular side branches, and finally end in thin, branched filaments. The later lead growths are, in fact, characteristic of progressively more dilute lead gels, and are presumably due to impoverishment of the lower portion of the gel with respect to lead. This effect is again apparent in trees prepared by reduction with zinc, in which the flat, sword-like growths of high lead concentrations degenerate at the bottom of the tube into the fine, cross filament type which appears as the initial growth only at low lead concentrations. Experiment No. 3, Series VI, is of special interest in this connexion. In this example, growth was initiated from both ends of the gel and took place to an equal extent in each case, gravity thus having no effect. The two trees changed in type quickly from the striking, tight spiral structure to the fine, irregular, branched type—a transition which usually takes place gradually over the whole length of a tube—within a distance of a few inches. Presumably this is due to the double growth which uses up the lead acetate more quickly than a single tree and removes it by osmotic means from the middle of the tube, in both directions. Thus, although the fine branches of the later growth met in the middle of the tube, there was no overlapping of the two structures. It appears, therefore, that although the initial growth of the lead tree depends essentially on the lead concentration of the gel in which it is grown, the modifications of structure which take place after the first growth period are caused by the *change* in concentration of the lead from the lower part of the gel to the lead-impoverished region in the neighbourhood of the growing tip. The upper part of the gel in which the primary stages of growth took place probably becomes entirely free from dissolved lead, as the initial structure does not increase or modify during the later stages of growth.

## SUMMARY OF RESULTS.

(1) The work of previous investigators on metal trees is summarised.

(2) It is found that tin displaces lead from lead acetate in silica gels but not from lead nitrate in gels under the same conditions.

(3) The morphology of lead trees grown by tin reduction is fundamentally dependent on the concentration of lead in the gel, widely different growth types being produced.

(4) A new spiriform type of growth is described.

(5) The effect of the quantity of acetic acid in the gel mixture is unimportant in modifying the morphology, as the system is efficiently buffered.

(6) The formation of a lead tree by means of the action of tin in the silica–acetate system does not take place in the sol.

(7) Visible tree formation commences immediately on gelation.

(8) The rate of growth of the lead tree is initially rapid, but slows down owing to impoverishment of the gel with respect to lead and to increase in the size of the electrochemical circuit.

(9) The growth of lead trees in lead acetate impregnated silica gel can be induced by reduction with zinc, aluminium, magnesium, manganese, chromium, cadmium, iron, and copper, but not with nickel or cobalt.

(10) The morphology of the lead trees produced by metals far removed from lead in the electrochemical series is somewhat similar, and spiriform growths are not produced.

(11) Colloidal materials in the gel have an unpredictable inhibiting or modifying influence on the structure of the lead trees.

London, Imperial College and
Shoreditch Technical Institute. [*Received, February 28th,* 1938.]

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## 115. *The Preparation and Therapeutic Properties of Certain Acridine Derivatives. Part II. Derivatives of* s-(6-*Amino*-2-*quinolyl*)-5-*acridylethenes.*

By W. L. Glen, M. M. J. Sutherland, and F. J. Wilson.

With a Note on Trypanocidal Action by C. H. Browning, P. Browning, R. Gulbransen, and J. V. M. Robb.*

*For reasons discussed in the theoretical part of this paper, it was decided to introduce* into the quinolylacridylethenes described in Part I amino-, acetamido-, and dimethylamino-groups in position 6 of the quinoline part of the molecule. A series of such compounds was prepared in the form of quaternary salts and examined for trypanocidal action in mice infected experimentally with *T. brucei*. In general, the compounds showed trypanocidal action, which is discussed, the results being marked with s-(6-*amino-2-quinolyl methochloride*)-5-*acridylethene hydrochloride*, s-(6-*acetamido-2-quinolyl methosulphate*)-5-(*acridyl methosulphate*)*ethene*, and s-(6-*acetamido-2-quinolyl methochloride*)-5-(*acridyl methochloride*)*ethene*.

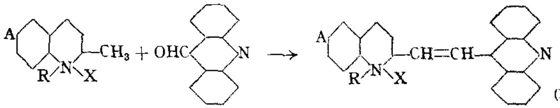
In Part I (J., 1936, 1484) the quinolylacridylethene series was investigated and we next considered the introduction of substituents into the molecule.

It had been found by Browning, Cohen, and their co-workers that, while quinolyl styryl compounds tended to show therapeutic action in animals experimentally infected with trypanosomes, this property was especially marked when there were present simultaneously a free amino-group, either in the benzene or the quinoline nucleus, and an acylamido-group in the other nucleus (*Proc. Roy. Soc.*, 1929, *B*, **105**, 99; 1933, *B*, **113**, 293). Accordingly, we decided in the first place to incorporate one such group. The orientation of the substituent groups in the quinoline nucleus had also been shown to be of great importance; *e.g.*, *s*-(6-acetamido-2-quinolyl methosulphate)-*p*-dimethylaminophenylethene or the corresponding methochloride is a powerful trypanocide, whereas the 7-acetamido-isomer is less active and the 4-isomer (methochloride) has no action in similar doses.

* Working in the Bacteriological and Pathological Department of the University and Western Infirmary, Glasgow, with the support of the Medical Research Council and during the tenure of a Muirhead Scholarship by J. V. M. R.

Accordingly, a series of quinolylacridylethene derivatives containing amino-, acetamido-, and dimethylamino-groups in position 6 of the quinoline portion of the molecule was prepared and examined.

The following compounds were prepared by condensing the appropriate quinaldine alkiodide with acridine-5-aldehyde in a solvent with piperidine as catalyst :


(I.)

(1) s-(6-*Acetamido-2-quinolyl methiodide*)-5-*acridylethene* (I; A = NHAc, RX = MeI) which was converted into the corresponding (2) *methochloride* by means of silver chloride and then by deacetylation with boiling hydrochloric acid into the *hydrochloride* of (3) s-(6-*amino-2-quinolyl methochloride*)-5-*acridylethene* (I; A = $NH_2$, RX = MeCl); treatment of (1) with excess of methyl sulphate gave (4) s-(6-*acetamido-2-quinolyl methosulphate*)-5-(*acridyl methosulphate*)*ethene* (as I; A = NHAc, RX = $Me_2SO_4$), which with sodium chloride gave (5) the corresponding *dimethochloride*; (6) s-(6-*acetamido-2-quinolyl ethiodide*)-5-*acridylethene* (I; A = NHAc, RX = EtI), from which by means of silver chloride the corresponding (7) *ethochloride* was prepared and thence by deacetylation with boiling hydrochloric acid the *hydrochloride* of (8) s-(6-*amino-2-quinolyl ethochloride*)-5-*acridylethene* (I; A = $NH_2$, RX = EtCl); (9) s-(6-*acetamido-2-quinolyl metho*-p-*toluenesulphonate*)-5-*acridylethene* (I; A = NHAc, RX = $C_6H_4Me{\cdot}SO_3Me$) and then converted into the (10) 5-(*acridyl methosulphate*)*ethene*; (11) s-(6-*dimethylamino-2-quinolyl methiodide*)-5-*acridylethene* (I; A = $NMe_2$, RX = MeI) and from this the corresponding (12) *methochloride* and its *hydrochloride*.

*Trypanocidal Action*.—The above compounds were examined for trypanocidal action in mice infected experimentally with *T. brucei*. The procedure followed was that described by Browning *et al.* (*loc. cit.*). The results are in the following table, those with 6-dimethylaminoquinaldine methochloride and *s*-(6-dimethylamino-2-quinolyl methochloride)phenylethene, from the paper cited, together with *s*-(2-quinolyl methosulphate)-5-(acridyl methosulphate)ethene and *s*-(2-quinolyl methochloride)-5-(acridyl methochloride)ethene, from Part I of this series, being added for comparison. Treatment was administered 24 hours after inoculation, when scanty trypanosomes were present in the blood; it consisted in a single subcutaneous injection of an aqueous solution of the substance. The dose of each substance, except when limited by solubility, approached the maximum tolerated without general toxic effects by uninfected animals.

| Substance. | Dose, mg. per 20 g. mouse. | Therapeutic result. |
|---|---|---|
| (3) Hydrochloride | 2·5 * | Marked |
| (4) | 10 | Marked |
| (5) | 10 | Marked |
| (8) Hydrochloride | 1·7 | Trace—*slight* |
| (10) | 1·7 * | Trace—slight |
| (12) Hydrochloride | 1·7 | Trace—slight |
| 6-Dimethylaminoquinaldine methochloride | 0·18 | 0 |
| *s*-(6-Dimethylamino-2-quinolyl methochloride)phenylethene | 0·1 | 0 |
| *s*-(2-Quinolyl methosulphate)-5-(acridyl methosulphate)ethene | 3·3 | 0 |
| *s*-(2-Quinolyl methochloride)-5-(acridyl methochloride)ethene | 10 | 0 |

* Dose limited by solubility.
"Trace"—prolongation of life for several days beyond that of the untreated controls.
"Slight"—disappearance of parasites from the blood for several days to a week.
"Marked"—absence of parasites from the blood for 10 days or longer.
(Untreated control animals died in 3 or 4 days after inoculation.)

*Conclusions*.—In general, these compounds showed trypanocidal action. The insolubility of several of them (nos. 3, 5, and 10) prevented the administration of sufficiently large doses to obtain maximum effects. The results suggest that, with the quinolylacridylethenes prepared by us, the introduction of an amino- or an acetamido-group in position 6

of the quinoline nucleus produces trypanocidal activity. Further, the activity is due in part to the acridine portion of the molecule, since 6-dimethylaminoquinaldine methochloride and *s*-(6-dimethylamino-2-quinolyl methochloride)phenylethene (Browning *et al.*, *loc. cit.*), which both have a 6-amino-group, and the latter also the ethene linkage, are much more toxic for the mammalian host and do not exert trypanocidal action in doses approaching the maximum tolerated.

This work is being continued. It is hoped to publish shortly an account of investigations on compounds with an amino-group in position 4 of the quinoline nucleus.

## Experimental.

6-Aminoquinaldine and its derivatives were prepared by the methods described by Hamer (J., 1921, **119**, 1432) and Browning, Cohen, Ellingworth, and Gulbransen (*Proc. Roy. Soc.*, **1924**, *B*, **96**, 325). The 6-nitroquinaldine, previously thoroughly washed, was purified through the nitrate (charcoal), the minimum amount of dilute nitric acid being used to avoid formation of tar as much as possible; the free base (pale yellow) was precipitated by aqueous ammonia, added till the solution was alkaline to Congo-paper but acid to litmus to avoid contamination by a red impurity. 6-Aminoquinaldine can be conveniently purified through the tartrate (yellow needle-shaped prisms from water), precipitated by mixing alcoholic solutions of the base and tartaric acid, 6-nitroquinaldine giving no precipitate. The yield of 6-acetamidoquinaldine methiodide is slightly improved by using 25% excess of methyl iodide and heating for 2 hours on the water-bath. 6-*Acetamidoquinaldine ethiodide*, prepared by refluxing 10 g. of 6-acetamidoquinaldine and 5 c.c. of ethyl iodide in 50 c.c. of nitrobenzene for 2 hours on the water-bath and then cooling, crystallised from aqueous alcohol in yellow prisms, m. p. 265—270° (decomp.), after darkening at about 250° (Found: N, 8·1. $C_{14}H_{17}ON_2I$ requires N, 7·9%).

s-(6-*Acetamido-2-quinolyl methiodide*)-5-*acridylethene* (1), prepared by refluxing on the water-bath for 2 hours a filtered solution of 10·7 g. of 6-acetamidoquinaldine methiodide and 8 g. of acridine-5-aldehyde in 80 c.c. of alcohol and 30 c.c. of water with 5 drops of piperidine, was collected hot and purified by repeated extraction with hot alcohol; yield, 80%. It was a red crystalline powder, m. p. 233—240° (decomp.) after darkening at about 140°, insoluble or almost insoluble in the usual solvents, including water, moderately soluble in nitrobenzene, from which it separated crystalline (Found: N, 8·1, 8·1. $C_{27}H_{22}ON_3I$ requires N, 7·9%). It was converted into the corresponding *methochloride* (2) by repeated boiling for several hours with a suspension of freshly precipitated silver chloride in aqueous methyl alcohol; the filtrate was concentrated, and the orange powder recrystallised from methyl alcohol. The substance darkened at 190° and melted at 220—228° (decomp.) (Found: N, 9·5. $C_{27}H_{22}ON_3Cl$ requires N, 9·6%).

s-(6-*Amino-2-quinolyl methochloride*)-5-*acridylethene hydrochloride* (3), prepared by boiling (2) with concentrated hydrochloric acid and a little water for 3—4 hours and treating the cold solution with dilute aqueous sodium carbonate to reduce the acidity somewhat, crystallised from methyl alcohol containing a little water in dark red prisms, m. p. 205—210° (decomp.), after darkening at about 180°. It dissolved readily in water or ethyl alcohol and after diazotisation yielded a dye with β-naphthol (Found: N, 9·6. $C_{25}H_{20}N_3Cl,HCl$ requires N, 9·7%).

s-(6-*Acetamido-2-quinolyl methosulphate*)-5-(*acridyl methosulphate*)*ethene* (4) was prepared by heating at 120°, and then at 130—140° for 25 minutes, 9 g. of (1) in 30 c.c. of nitrobenzene with 7 c.c. (large excess) of methyl sulphate. After standing overnight, the orange-red powder was recrystallised twice from alcohol containing a little water; it darkened at 200° and melted at 225—235° (decomp.), contained no halogen, and dissolved readily in water or alcohol (Found: N, 6·4. $C_{30}H_{31}O_9N_3S_2$ requires N, 6·5%). The corresponding *dimethochloride* (5), prepared in the usual way by adding a saturated sodium chloride solution to a hot aqueous solution of the substance and allowing it to cool, formed an orange precipitate, which was recrystallised first from water and then from aqueous alcohol, in which solvents it dissolved readily (Found: N, 8·5. $C_{28}H_{25}ON_3Cl_2$ requires N, 8·6%). The dimethonitrate (orange) and dimethiodide (dark red) can be prepared similarly.

s-(6-*Acetamido-2-quinolyl ethiodide*)-5-*acridylethene* (6) was prepared from 6-acetamidoquinaldine ethiodide as with (1), the heating being from 3—3½ hours; it was purified by extraction with hot alcohol (yield, 70%). The dried substance was reddish-orange, but on exposure to air or on moistening with alcohol it became yellowish-brown, presumably owing to solvation. It darkened at about 235° and melted at about 238° (decomp.) and in solubility resembled (1)

(Found: N, 7·8. $C_{28}H_{24}ON_3I$ requires N, 7·7%). It was converted by silver chloride in the usual way into the corresponding ethochloride (7), an orange mass, which was converted into s-(*6-amino-2-quinolyl ethochloride*)-*5-acridylethene hydrochloride* (8) as with (3). This substance crystallised from 60% aqueous alcohol in dark red, needle-shaped prisms, m. p. 280—300° (decomp.), readily soluble in water and alcohol (Found: N, 9·5. $C_{28}H_{22}N_3Cl,HCl$ requires N, 9·4%).

s-(*6-Acetamido-2-quinolyl metho-*p*-toluenesulphonate*)-*5-acridylethene* (9) was prepared by refluxing on the water-bath for 3 hours 9·3 g. of 6-acetamidoquinaldine metho-*p*-toluenesulphonate * and 6·1 g. of acridine-5-aldehyde in 75 c.c. of alcohol with 8 drops of piperidine. The product was collected hot, extracted with hot alcohol, and recrystallised from aqueous alcohol (yield, 5·6 g.). The yellow crystalline powder, darkening at about 240° and melting at about 250° (decomp.), was moderately easily soluble in hot water and sparingly soluble in alcohol (Found: N, 7·4. $C_{34}H_{29}O_4N_3S$ requires N, 7·3%). The corresponding methochloride (orange-yellow) and methiodide (dark red) were obtained by precipitating aqueous solutions with sodium chloride and potassium iodide.

s-(*6-Acetamido-2-quinolyl metho-*p*-toluenesulphonate*)-*5-*(*acridyl methosulphate*)*ethene* (10) was prepared by heating first at 100° and then at 120—130° for ½ hour 3·7 g. of (9) with 0·8 c.c. of methyl sulphate in 23 c.c. of nitrobenzene. The product, collected after standing overnight, was washed with alcohol and ether and recrystallised from aqueous alcohol, from which it separated in small orange-yellow needles, m. p. 245—248° (decomp.), after darkening at about 240° (Found: C, 62·0; H, 5·3; S, 8·8. $C_{36}H_{35}O_8N_3S_2$ requires C, 61·6; H, 5·0; S, 9·1%). It was moderately easily soluble in alcohol, and soluble in water, from which solution the dimethochloride (orange) and the dimethiodide (orange-red) could be precipitated in the usual way.

s-(*6-Dimethylamino-2-quinolyl methiodide*)-*5-acridylethene* (11) was prepared by boiling for 4 hours a solution of 2 g. of 6-dimethylaminoquinaldine methiodide and 1·5 g. of acridine-5-aldehyde in 30 c.c. of alcohol with 4 drops of piperidine. The product (yield, 60%), collected hot and extracted with hot alcohol, was a dark red, crystalline powder moderately easily soluble in methyl and ethyl alcohols, sparingly soluble in hot water (Found: I, 25·0. $C_{27}H_{24}N_3I$ requires I, 24·5%). It was converted in the usual way by silver chloride in methyl alcohol into the corresponding *methochloride* (12), a red crystalline substance, m. p. 200—210° (decomp.) after darkening at about 150°, moderately easily soluble in hot water (Found: N, 10·0. $C_{27}H_{24}N_3Cl$ requires N, 9·9%). This methochloride was converted, by solution in a little dilute hydrochloric acid, followed by cooling, into the hydrochloride, which crystallised from methyl alcohol as a very dark purple powder, decomposing at about 220° but not completely melted at 300°, and readily soluble in water or alcohol.

We thank the Governors of this College for a Research Assistantship awarded to one of us (W. L. G.), and Imperial Chemical Industries, Ltd., for a research grant.

"Freeland" Chemical Laboratories,
The Royal Technical College, Glasgow. [*Received, February 24th*, 1938.]

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## 116. *Experiments on the Synthesis of Local Anæsthetics. Part III.*

By S. Bagchee, K. N. Gaind, and J. N. Rây.

Esters of α-diethylamino- or α-piperidino-β-acyloxy-β-phenylpropionic acid have been prepared. The benzoyloxy-, cinnamoyloxy-, and β-phenylpropoxy-compounds described showed local anæsthetic activity.

Substances of the formula (I) have been prepared in connexion with the problem whether an unsaturated centre is necessary for a compound to produce local anæsthesia.

$$\text{(I.)}\quad (p)R\cdot C_6H_4\cdot CH(O\cdot COR')\cdot CHR''\cdot CO_2R'''$$

α-Bromo-β-hydroxy-β-phenylpropionic acid was esterified with various alcohols, the resulting esters condensed with diethylamine or piperidine, and the α-diethylamino- or α-piperidino-β-hydroxy-β-phenylpropionates acylated. The hydrochlorides of the compounds (I) where R = H, R′ = Ph, CH:CHPh, or $CH_2\cdot CH_2Ph$, R″ = $C_5H_{10}N$, and R‴ = Me were prepared. All the compounds had local anæsthetic properties in different degrees.

* M. p. not recorded in literature; we found 209—211°.

*iso*Propyl α-piperidino-β-cinnamoyloxy-β-phenylpropionate gives a *hydrochloride* which is not very stable to water and has only feeble local anæsthetic properties. The corresponding *benzoyloxy*-derivative shows much more activity, a drop of a 1% solution placed on the tip of the tongue causing a tingling sensation lasting for several minutes. The *hydrochloride* of methyl α-piperidino-β-β′-phenylpropoxy-β-phenylpropionate is a local anæsthetic markedly weaker than the corresponding *benzoyloxy*-derivative; the related cinnamoyloxy-compound is undoubtedly weaker than either of them, a drop of a 1% solution causing only a slight anæsthesia.

The detailed examination of these compounds will be described elsewhere.

## Experimental.

α-Bromo-β-hydroxy-β-phenylpropionic acid was prepared by the method of Read and Williams (*J. Proc. Roy. Soc. N.S. Wales*, 1917, **51**, 558). From 55 g. of cinnamic acid, α-bromo-β-hydroxy-β-phenylpropionic acid (45 g.), αβ-dibromo-β-phenylpropionic acid (6 g.), and ω-bromostyrene (5 g.) can be obtained if the acid is brominated in a solution of sodium carbonate (27 g.) in water (800 c.c.). Departure from these relative proportions results in much diminished yields.

*Methyl α-Bromo-β-hydroxy-β-phenylpropionate.*—The acid (20 g.) was refluxed in dry methyl alcohol (45 c.c.) containing hydrogen chloride (*ca.* 3%) for 8 hours, matter volatile in a vacuum at 100° removed, and the residue washed with sodium bicarbonate solution. The *methyl* ester, isolated by means of ether, crystallised from light petroleum in plates (18·3 g.), m. p. 64° (Found: C, 46·6; H, 4·2; Br, 30·7. $C_{10}H_{11}O_3Br$ requires C, 46·3; H, 4·2; Br, 30·9%).

The ethyl, propyl, *iso*propyl, butyl, *iso*butyl, *iso*amyl, and benzyl esters, similarly prepared, were viscous liquids which could not be distilled in a high vacuum without decomposition. The crude esters were used after removal of unchanged acid and all matter volatile at 100° in a vacuum.

*Methyl α-Piperidino-β-hydroxy-β-phenylpropionate.*—A mixture of methyl α-bromo-β-hydroxy-β-phenylpropionate (10 g.), piperidine (7 g.), and benzene (50 c.c.) was heated on the steam-bath for 4 hours. The filtrate after the removal of piperidine hydrochloride was freed from the solvent, and the residue extracted with ether. The pasty mass obtained after the removal of ether solidified in contact with light petroleum at 0°; it then crystallised from this solvent in glancing needles, m. p. 142° (Found: N, 5·5. $C_{15}H_{21}O_3N$ requires N, 5·3%). The *hydrochloride*, prepared in ethereal solution, crystallised from acetone–ether in needles, m. p. 182° (Found: N, 4·35; Cl, 11·6. $C_{15}H_{21}O_3N,HCl$ requires N, 4·7; Cl, 11·8%).

Propyl α-piperidino-β-hydroxy-β-phenylpropionate, prepared similarly, was a viscous liquid, which was characterised as its benzoyl derivative (below).

iso*Propyl α-piperidino-β-hydroxy-β-phenylpropionate* had m. p. 111° after crystallisation from light petroleum (Found: N, 4·7. $C_{17}H_{25}O_3N$ requires N, 4·8%). The *hydrochloride* of *iso*butyl α-piperidino-β-hydroxy-β-phenylpropionate had m. p. 141° (Found: N, 4·2; Cl, 10·2. $C_{18}H_{27}O_3N,HCl$ requires N, 4·1; Cl, 10·4%). iso*Amyl α-piperidino-β-hydroxy-β-phenylpropionate* formed plates, m. p. 86°, from dilute methyl alcohol (Found: N, 4·45. $C_{19}H_{29}O_3N$ requires N, 4·4%). The *hydrochloride*, m. p. 159°, crystallised from acetone–ether (Found: N, 4·0; Cl, 9·9. $C_{19}H_{29}O_3N,HCl$ requires N, 3·9; Cl, 9·9%). Benzyl α-piperidino-β-hydroxy-β-phenylpropionate was purified *via* its *hydrochloride*, which crystallised from acetone in needles, m. p. 187° (Found: N, 3·95; Cl, 9·45. $C_{21}H_{25}O_3N,HCl$ requires N, 3·7; Cl, 9·2%).

*Hydrochloride of Methyl α-Piperidino-β-benzoyloxy-β-phenylpropionate.*—A mixture of methyl α-piperidino-β-hydroxy-β-phenylpropionate (1·0 g.), benzoyl chloride (0·5 c.c.), and benzene (5 c.c.) was heated for 4 hours. After the removal of the solvent, the residue was heated at 100° for 3 hours. The product was dissolved in acetone and precipitated with dry ether; the *hydrochloride* then crystallised from acetone–ether in clusters of radiating needles, m. p. 101° (Found: N, 2·7; Cl, 8·6. $C_{22}H_{25}O_4N,HCl$ requires N, 2·8; Cl, 8·8%).

The *hydrochloride* of ethyl α-piperidino-β-benzoyloxy-β-phenylpropionate, prepared similarly and crystallised from acetone–ether, had m. p. 127° (Found: N, 3·4; Cl, 8·3. $C_{23}H_{27}O_4N,HCl$ requires N, 3·35; Cl, 8·5%).

The *hydrochloride* of propyl α-piperidino-β-benzoyloxy-β-phenylpropionate, m. p. 112°, was purified by dissolving the crude product of benzoylation in dry acetone (charcoal) and precipitating it with dry ether; it crystallised from acetone–ether in clusters of rod-like needles (Found: N, 3·0; Cl, 8·0. $C_{24}H_{29}O_4N,HCl$ requires N, 3·2; Cl, 8·2%).

The *hydrochloride* of butyl α-piperidino-β-benzoyloxy-β-phenylpropionate, crystallised from

acetone–alcohol, had m. p. 118° (Found : N, 3·0; Cl, 7·9. $C_{22}H_{31}O_4N,HCl$ requires N, 3·1; Cl, 7·9%).

iso*Butyl α-piperidino-β-benzoyloxy-β-phenylpropionate* was prepared by heating the hydroxy-compound in pyridine solution with benzoyl chloride at 100° for 3 hours. The product, precipitated by water, solidified when kept at 0° for 12 hours. It crystallised from dilute methyl alcohol in needles, m. p. 82° (Found : N, 3·7. $C_{25}H_{31}O_4N$ requires N, 3·4%).

iso*Amyl α-piperidino-β-benzoyloxy-β-phenylpropionate*, prepared similarly, crystallised from dilute alcohol in needles, m. p. 79° (Found : N, 3·3. $C_{26}H_{33}O_4N$ requires N, 3·5%).

The *hydrochloride* of benzyl α-piperidino-β-benzoyloxy-β-phenylpropionate had m. p. 175° (Found : N, 3·0; Cl, 7·3. $C_{28}H_{29}O_4N,HCl$ requires N, 2·9; Cl, 7·3%).

*Hydrochloride of Methyl α-Piperidino-β-β′-phenylpropoxy-β-phenylpropionate.*—A mixture of methyl α-piperidino-β-hydroxy-β-phenylpropionate (0·5 g.) and β-phenylpropionyl chloride (1 c.c.) was heated at 120—130° for 4 hours. The product was cooled in ice and stirred with dry ether. The precipitated *hydrochloride*, crystallised from acetone–ether, had m. p. 197° (decomp.) (Found : N, 3·1; Cl, 8·1. $C_{24}H_{29}O_4N,HCl$ requires N, 3·2; Cl, 8·2%).

The related cinnamoyloxy-compound, prepared as above, could not be satisfactorily crystallised on account of its highly hygroscopic nature.

The *hydrochloride* of *iso*propyl α-piperidino-β-benzoyloxy-β-phenylpropionate, prepared in an analogous manner, had m. p. 190° (decomp.) after crystallisation from ethyl acetate–ether (Found : N, 3·05; Cl, 8·1. $C_{24}H_{29}O_4N,HCl$ requires N, 3·2; Cl, 8·2%).

The related cinnamoyloxy-derivative was prepared by heating a mixture of *iso*propyl α-piperidino-β-hydroxy-β-phenylpropionate (0·5 g.) and cinnamoyl chloride (0·7 g.) at 175° for 3 hours. The *hydrochloride*, isolated in the usual manner, crystallised from acetone–dry ether in fine needles, m. p. 223° (Found : N, 2·7; Cl, 8·0. $C_{26}H_{31}O_4N,HCl$ requires N, 3·0; Cl, 7·8%).

*α-Bromo-β-hydroxy-β-*p*-nitrophenylpropionic Acid.*—To a solution of sodium carbonate (12 g.) in water (400 c.c.), well-powdered *p*-nitrocinnamic acid (25 g.) was added with stirring, the solution was cooled to 0°, and bromine (15 c.c.), vaporised with air, was led in. After 2 hours, the separated ω-bromo-*p*-nitrostyrene was removed, and the aqueous filtrate shaken with light petroleum to remove free bromine. The acidified solution furnished the *bromo-hydroxy-acid*, which crystallised from water in needles (22 g.), m. p. 179° (Found : N, 4·8; Br, 27·7. $C_9H_8O_5NBr$ requires N, 4·8; Br, 27·5%). The *ethyl* ester, m. p. 95°, crystallised from ligroin (Found : N, 4·6; Br, 25·3. $C_{11}H_{12}O_5NBr$ requires N, 4·6; Br, 25·1%).

Ethyl α-piperidino-β-hydroxy-β-*p*-nitropheuylpropionate was prepared by a method similar to that used for methyl α-piperidino-β-hydroxy-β-phenylpropionate and purified by conversion into its *hydrochloride*, m. p. 205° (decomp.) after crystallisation from acetone–ether (Found : N, 7·8; Cl, 9·8. $C_{16}H_{22}O_5N_2,HCl$ requires N, 7·8; Cl, 9·9%).

The foregoing substance was benzoylated in pyridine solution at 100° for 3 hours. The *benzoyl* derivative crystallised from alcohol in pale yellow needles, m. p. 139° (Found : N, 6·5. $C_{23}H_{26}O_6N_2$ requires N, 6·6%); its *hydrochloride* had m. p. 193° (Found : N, 5·9; Cl, 7·9. $C_{23}H_{26}O_6N_2,HCl$ requires N, 6·1; Cl, 7·6%).

*Ethyl α-Piperidino-β-benzoyloxy-β-*p*-aminophenylpropionate.*—The above nitro-compound (0·5 g.) was reduced with a platinum oxide catalyst (0·05 g.) for 4 hours. After the removal of the solvent, the product was converted by ethereal hydrogen chloride into its *dihydrochloride*, which crystallised from acetone–ether in long needles, m. p. 113° (decomp.) (Found : N, 6·0; Cl, 15·0. $C_{23}H_{28}O_4N_2,2HCl$ requires N, 6·0; Cl, 15·1%).

*Methyl α-Diethylamino-β-hydroxy-β-phenylpropionate.*—Prepared in the same manner as the corresponding piperidino-compouud, this substance was purified *via* its *hydrochloride*, which crystallised from ether–methyl alcohol in needles, m. p. 187° (decomp.) (Found : Cl, 12·3. $C_{14}H_{21}O_3N,HCl$ requires Cl, 12·3%).

*Propyl α-diethylamino-β-hydroxy-β-phenylpropionate hydrochloride*, m. p. 147° (Found : N, 4·1; Cl, 11·2. $C_{16}H_{25}O_3N,HCl$ requires N, 4·1; Cl, 11·25%), and iso*propyl α-diethylamino-β-hydroxy-β-phenylpropionate hydrochloride*, m. p. 181° (Found : Cl, 11·2. $C_{16}H_{25}O_3N,HCl$ requires Cl, 11·25%), were similarly prepared.

Our thanks are due to Dr. K. S. Narang for the analyses of nitrogen, which were done by the micro-method.

Punjab University, Lahore. [*Received, December 13th*, 1937.]

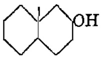
# 117. *Fused Carbon Rings. Part XIV. Synthesis of Dicyclic Compounds with an Angular Methyl Group from Substances containing a* n-*Pentenyl Side Chain.*

By G. H. Elliott and R. P. Linstead.

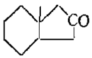
The general object was a model synthesis of the 8-methyl-1-hydrindanone type of structure, met with in many sexual hormones. An earlier synthetic method, involving the ring closure of butenyl side chains containing a terminal double bond, gave β- and not α-ketones. Analogous experiments have now been carried out with compounds containing pentenyl side chains. A new synthesis of 8-methyl-1-hydrindanone is described, and a connection has been established between 9-methyl-1-decalone and 9-methyl-2- and -3-decalones.

In previous papers it has been shown that various butenyl-*cyclo*hexanols and -*cyclo*hexenes can be cyclised to derivatives of decalin (J., 1936, 470, 476; 1937, 1136, 1140; compare following paper), the method being well adapted for the synthesis of compounds containing an angular methyl group, for example, of 9-methyl-2-decalol (I), and thence of 8-methyl-2-hydrindanone (II). One of the general objects of this series of investigations is the synthesis of sexual hormones which contain the isomeric 8-methyl-1-hydrindanone structure (III) and in the present paper we have explored the possibility of modifying the earlier synthetic method in order to obtain compounds of this type.

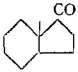
The use of compounds containing a $\Delta^{\delta}$-*n*-pentenyl side chain appeared promising for two reasons. 2-*Methyl*-1-$\Delta^{\delta}$-n-*pentenyl*cyclo*hexanol* (IV) might cyclise to yield 1 : 9-dimethyloctalin (either directly or through an alcohol). In this there seemed a reasonable possibility of the double bond approaching the 1-methyl group to yield at least a considerable proportion of the $\Delta^{1:2}$-form (V). Oxidation of this would then lead to 2-methyl*cyclo*hexane-2-carboxylic-1-propionic acid and thence to 8-methyl-1-hydrindanone (III).



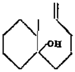
(I.)



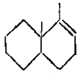
(II.)



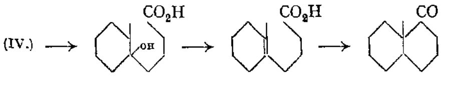
(III.)



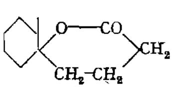
(IV.)


(V.)

The other possibility was that 2-methyl-1-$\Delta^{\delta}$-*n*-pentenyl*cyclo*hexanol (IV) could be oxidised to the hydroxy-acid (VI), which would yield γ-(2-methyl-$\Delta^{1}$-*cyclo*hexenyl)butyric acid (VII) on dehydration. As this acid has been converted into 9-methyl-1-octalone and thence into 9-methyl-1-decalone (VIII) by Chuang, Tien, and Ma (*Ber.*, 1936, **69**, 1494) and by Cook and Lawrence (J., 1937, 817), the synthetic possibilities were obvious.



(VI.) (VII.) (VIII.)



(IX.)

In practice, the first of these routes has so far proved of little value, but the second was successful.

Oxidation of methylpentenyl*cyclo*hexanol (IV) with potassium permanganate, followed by distillation of the product with oxalic acid, yielded a mixture of the desired unsaturated acid (VII), and a smaller amount of the isomeric spiro-*lactone* (IX), which we suspect to be a mixture of isomerides. Linstead and Rydon (J., 1933, 580) showed that a δ-lactone of similar structure, containing a quaternary δ-carbon atom, could be converted (reversibly) into an isomeric γδ-unsaturated acid at the boiling point. When the *spiro*-lactone (IX) was heated to 200°, there was a small development of acidity, but it appears that either the equilibrium is far on the lactone side or else the mobility is very low. The lactone (IX)

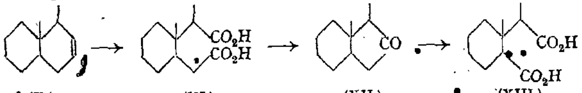
can, however, be converted into the unsaturated acid (VII) by esterification to the ester of (VI), dehydration, and hydrolysis.

As methylpentenyl*cyclo*hexanol can be made in one stage from the Grignard compound of the readily available $\Delta^3$-pentenyl bromide, the acid (VII) is easily prepared by this route as a crystalline solid, m. p. 44°. The identity of our product with those of previous workers (*loc. cit.*) follows from the agreement in the m. p. of the *p*-bromophenacyl ester with that of Chuang, Tien, and Ma, and from the results of cyclisation. The 9-methyl-1-octalone and -decalone (VIII) obtained from the acid by Cook and Lawrence's method (J., 1935, 1637) agreed in properties with the products of previous workers, and the semicarbazone of the saturated ketone was identical with the derivative prepared by Kon, Linstead, and Simons (J., 1937, 814). The reduction of the intermediate chloromethyldecalone, obtained from the acid chloride of (VII), was attempted by treatment with aluminium chloride and *cyclo*hexane, following Nenitzescu and Cantuniari (*Annalen*, 1934, **510**, 269). We obtained, however, only a poor yield of an unsaturated *ketone*, isomeric with the 9-methyl-1-octalone obtained by the usual method. The method does not appear to be applicable to this type of polycyclic chloro-ketone (compare Robinson and Walker, J., 1937, 61; Cook and Lawrence, *loc. cit.*, 1937).

Reduction of 9-methyl-1-decalone with aluminium *iso*propoxide gave 9-methyl-1-decalol (probably an epimeric mixture) in excellent yield, and this on oxidation with nitric acid gave 2-methyl*cyclo*hexane-2-carboxylic-1-β-propionic acid. As in previous work (Kon, Linstead, and Simons, *loc. cit.*; Robinson and Walker, J., 1937, 1160), the acid could not be obtained crystalline, but on distillation with baryta yielded 8-methyl-1-hydrindanone (III). The ketone was identical with the synthetic product of Kon, Linstead, and Simons, and, like it, gave on oxidation the 2-methyl*cyclo*hexane-2-carboxylic-1-acetic acid, m. p. 164°, of Linstead and Millidge (J., 1936, 478). The carboxy-propionic acid (and thence the methylhydrindanone) was also obtained by direct oxidation of 9-methyl-1-decalone.

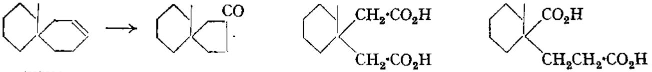
In previous work (Linstead, Millidge, and Walpole, J., 1937, 1140; Kon, Linstead, and Simons, *loc. cit.*) the following synthetic compounds containing an angular methyl group have been linked together by degradation: 9-methyl-2- and-3-decalones and 8-methyl-1- and -2-hydrindanones. To this list we can now add 9-methyl-1-decalone. These substances all have the same configuration, which, as has already been pointed out, is probably *cis*. This is supported by the physical properties of 9-methyl-1-decalone, which, it may be noted, was prepared by a process of reduction usually leading to a *cis*-configuration.

The other method of attack—the cyclisation of methylpentenyl*cyclo*hexanol (IV)—gave a series of products, of which the structures are not fully established, but those given below appear the most probable. When treated with a mixture of acetic and sulphuric acids and acetic anhydride (Linstead, Millidge, and Walpole, *loc. cit.*), the alcohol (IV) gave the acetate of an isomeric dicyclic secondary *alcohol*, $C_{12}H_{22}O$ (? 1 : 9-dimethyl-2- or -3-decalol), together with a dicyclic olefin, $C_{12}H_{20}$, probably a 1 : 9-dimethyloctalin (*e.g.*, X). Oxidation of the dicyclic alcohol with chromic acid yielded the corresponding *ketone*, $C_{12}H_{20}O$ (? 1 : 9-dimethyl-2- or -3-decalone), and its dehydration gave an *olefin*, $C_{12}H_{20}$. Permanganate oxidation of the latter gave a dibasic *acid*, $C_{12}H_{20}O_4$, which was also obtained from the ketone by means of nitric acid. Attempted oxidation of the ketone with chromic and sulphuric acids yielded no keto-acid, such as might have been obtained from 1 : 9-dimethyl-2-decalone if Wallach and Franke's oxidation of 2-methyl*cyclo*hexanone had been paralleled (*Annalen*, 1903, **329**, 376). Pyrolysis of the acid $C_{12}H_{20}O_4$ with baryta readily yielded a *ketone*, $C_{11}H_{18}O$, which was in turn oxidised to an *acid*, $C_{11}H_{18}O_4$. These products could correspond with the oxidation of a 1 : 9-dimethyl-$\Delta^{2:3}$-octalin (X), thus:




(X.) (XI.) (XII.) (XIII.)

On the other hand, the possibility that the dicyclic substances mentioned above are wholly or partly *spiro*-compounds cannot be excluded. For example, the olefin might be (XIV), in which case the $C_{11}$-ketone would be (XV). We have proved that the $C_{11}$-acid is *not* 2-methyl*cyclo*hexane-1 : 1-diacetic acid (XVI) by direct comparison with authentic material, but there remains a possibility that it is an isomeric carboxy-propionic acid (XVII).




(XIV.) (XV.) (XVI.) (XVII.)

The dicyclic olefin (X or XIV) evolved no hydrogen at the boiling point over an active platinum catalyst. This proves the presence of a quaternary carbon atom (Linstead, Millidge, Thomas, and Walpole, J., 1937, 1146), and excludes the presence of derivatives of 1 : 5-dimethyldecalin, formed by cyclisation of the pentenyl side chain away from the methyl group. At 335°, in the vapour phase over palladised asbestos, the olefin yielded a mixture of dimethylnaphthalenes. Dehydrogenation of the ketone $C_{12}H_{20}O$ over palladised charcoal gave a phenol, apparently a methylnaphthol, but in amount insufficient for identification. This evidence supports the decalin structure rather than the spiran, but we do not regard it as conclusive. As no evidence was obtained of the presence of olefin with the double bond in the desired $\Delta^{1:2}$-position (V) (which was the primary objective), the study of the substances obtained in these cyclisations has been temporarily discontinued in favour of more promising lines of attack.

While pentenyl bromide was under study, the opportunity was taken of confirming, from another angle, the synthesis of 1 : 1-dimethyl*cyclo*hexene from dimethyl-$\Delta^4$-*n*-pentenylcarbinol (Hibbit and Linstead, J., 1936, 470). In the earlier work this carbinol was prepared from ethyl $\Delta^5$-*n*-hexenoate and methylmagnesium iodide. We have now prepared it in excellent yield from the Grignard compound of $\Delta^4$-*n*-pentenyl bromide and acetone. The product was cyclised by means of phosphoric acid to dimethyl*cyclo*hexene, and this was oxidised to ββ-dimethyladipic acid, in agreement with the earlier work.

## EXPERIMENTAL.

The preparation of $\Delta^4$-*n*-pentenyl bromide essentially followed that of Paul (*Bull. Soc. chim.*, 1935, 2, 745) and Gaubert, Linstead, and Rydon (J., 1937, 1971). In the preparation of $\Delta^4$-*n*-pentenol by the action of sodium on tetrahydrofurfuryl chloride, better yields (90%, optimum 96%) were obtained by allowing the mixture to reflux with vigorous stirring overnight rather than for 1 hour.

*Preparation and Cyclisation of* 1 : 1-*Dimethyl*-$\Delta^4$-n-*pentenylcarbinol*.—A mixture of 72 g. of pentenyl bromide and 250 c.c. of ether was added to 12 g. of magnesium and 100 c.c. of ether, and, after the completion of the reaction, 29 g. of dry acetone in 150 c.c. of ether were added during 1 hour. After an hour's refluxing, the product was decomposed as usual and dried with potassium carbonate. The carbinol (48 g., 80%) had b. p. 61—66°/13 mm., $d_{4°}^{14·3°}$ 0·8346, $n_{D}^{14·3°}$ 1·4387, $[R_L]_D$ 40·36 (calc. for $|_1^{=}$, 40·31) (Found : C, 75·1; H, 12·6. Calc. : C, 74·9; H, 12·6%). The carbinol (17 g.) was cyclised under Hibbit and Linstead's conditions (*loc. cit.*) with 84 c.c. of phosphoric acid, the mixture finally being heated at 135—140° for 1·5 hours. The dimethyl*cyclo*hexene (55% yield, after redistillation over potassium) had b. p. 119—124°/752 mm., $d_{4°}^{16·2°}$ 0·8043, $n_{D}^{16·2°}$ 1·4474, $[R_L]_D$ 36·60 (calc. for $|_1^{=}$, 36·48). On oxidation with potassium permanganate it yielded ββ-dimethyladipic acid, m. p. and mixed m. p. 88°.

2-*Methyl*-1-$\Delta^\delta$-n-*pentenyl*cyclo*hexanol* (IV).—A mixture of 290 g. of pentenyl bromide and 400 c.c. of ether was added to a stirred mixture of 47 g. of activated magnesium and 400 c.c. of ether at such a rate that the solution boiled gently without external heating. The final mixture was refluxed for 40 minutes, treated slowly with 220 g. of 2-methyl*cyclo*hexanone in 400 c.c. of ether, and again refluxed for 40 minutes. The ethereal solution was decomposed with ice and aqueous ammonium chloride, and finally with dilute hydrochloric acid. The product was washed with water and aqueous sodium thiosulphate, dried with potassium carbonate, and isolated by distillation. 2-*Methyl*-1-$\Delta^\delta$-n-*pentenyl*cyclo*hexanol* has b. p. 122—124°/13 mm., $d_{4°}^{16·1°}$ 0·9164, $n_{D}^{16·1°}$ 1·4789, $[R_L]_D$ 56·56 (calc. for $|_1^{=}$, 56·48) (Found : C, 78·8; H,

12·1. $C_{13}H_{22}O$ requires C, 79·0; H, 12·2%). Yields of 57—68% were obtained, the best yields coming from bromide which had stood for some time over calcium chloride.

A mixture of 35 g. of this alcohol, 23 g. of sodium carbonate (anhydrous), and a little water was stirred at 0° and a total quantity of 2850 c.c. of 3% aqueous potassium permanganate was added in drops. The rate of addition was 5 c.c./min. for the first 2 hours, and subsequently 10 c.c./min. After standing overnight, the colourless supernatant liquid was decanted, the manganese mud washed with boiling water, and the combined aqueous solution evaporated to 200 c.c., acidified, and extracted with ether. The extract was dried thoroughly with sodium sulphate. Notwithstanding this, water separated when the ether had been removed and the residue was at 90°. Clearly this was due to a dehydration of the tertiary alcohol group catalysed by the acids formed in the oxidation. The products from the oxidation of 230 g. of alcohol were united, treated with 30 g. of anhydrous oxalic acid, and distilled at 7 mm. After a considerable and troublesome elimination of water, the residue distilled over as follows: (1) 145—151°, 43 g.; (2) 151—158°, 32 g.; (3) 158°, 15 g.; (4) 158—166°, 38 g.; (5) 166—175°, 4 g. Total 132 g. All the fractions were treated overnight with aqueous sodium bicarbonate and extracted with ether. The aqueous solution was acidified, and the organic acid isolated by means of ether and distilled. 67 G. of *γ-(2-methyl-Δ¹-cyclohexenyl)butyric acid* (VII) were so obtained, boiling at 166—167°/10 mm. and rapidly solidifying. The acid was very soluble in organic media, but crystallised from light petroleum (b. p. 40—60°) in thin waxy plates, m. p. 44°. Chuang, Tien, and Ma describe the acid as forming colourless needles, but give no m. p. (Found: C, 72·7; H, 10·0; equiv., 183·8. Calc.: C, 72·5; H, 10·0%; equiv., 182·2). The *p*-bromophenacyl ester formed glistening plates, m. p. 64° (Chuang *et al.* give 65—66°).

Fractional distillation of the non-acidic fraction yielded 31 g. of the spiro-*lactone* of *γ-(1-hydroxy-2-methyl*cyclo*hexyl)butyric acid* (IX), an oil with a lactonic odour, b. p. 145—155°/10 mm., and 20 g. more of the same unsaturated acid. The total direct yield of acid (VII) from tertiary alcohol was therefore 38%. The occurrence of acid in the lactone fraction was probably due to an isomeric change of a labile lactone on distillation. After redistillation, the lactone had b. p. 135°/1·5 mm. and was free of acid (Found: C, 72·3; H, 10·0. $C_{11}H_{18}O_2$ requires C, 72·5; H, 10·0%). The equivalent weight, determined by refluxing with excess of baryta and back-titration (Linstead, J., 1932, 115), was 185·0 (calc. 182·2). The stable lactone so obtained developed only 5% of acidity after 5 hours at 190°; at 230—240° decomposition occurred.

The structure of the lactone was proved by its conversion into the acid (VII) as follows: 31 G. of the lactone were refluxed for 5 hours with 100 c.c. of 10% alcoholic sulphuric acid. The product was poured into water and extracted with ether; the extract was washed with calcium chloride solution, dried, and freed from solvent. A solution of the hydroxy-ester so obtained (37 g.) in 250 c.c. of dry ether and 26 g. of pyridine (2 mols.) was treated at 0° with 24 g. of thionyl chloride (1·25 mols.) in drops. The product was filtered off, freed from solvent, and distilled. The ester so obtained (26 g., b. p. 124—126°/12 mm.) on hydrolysis with cold aqueous-alcoholic caustic potash yielded 10 g. of the solid acid (VII), b. p. 156—159°/5 mm., together with 10 g. of lactone. Dehydration of the hydroxy-ester with anhydrous oxalic acid was less successful.

γ-(2-Methyl-Δ¹-*cyclo*hexenyl)butyric acid (84 g.) was cyclised following Cook and Lawrence (*loc. cit.*). The intermediate chloro-ketone boiled at 130°/10 mm. and failed to give a satisfactory semicarbazone. It was dehalogenated as usual with dimethylaniline at 200°. The yield of 9-methyl-1-octalone, b. p. 108—111°/12 mm., was 47 g. (61%). The semicarbazone formed rather slowly at 30°; it crystallised in flattened needles, m. p. 228—229° (Chuang, 225—226°; Cook and Lawrence, 222—223°). Hydrogenation of the unsaturated ketone in pure acetic acid over Adams's platinum took only 1 hour and the temperature rose to 70°. The 9-methyl-1-decalone (probably *cis-*) so obtained boiled at 120—122°/20 mm. (46 g.). The semicarbazone, which formed slowly at 30°, rapidly on warming, had m. p. 210—216° (crude), 224° after crystallisation, not depressed by the semicarbazone of Kon, Linstead, and Simons (*loc. cit.*). The regenerated ketone, an oil with a camphoraceous odour, had b. p. 106°/9 mm., m. p. + 2°. The following physical properties accord well with those of Cook and Lawrence: $d_4^{16·2°}$ 0·9958, $n_D^{16·4°}$ 1·4926, $[R_L]_D$ 48·45 (calc., 48·61).

9-Methyl-1-decalone was reduced almost quantitatively by the Ponndorf–Verley method as follows: The ketone (44 g.) was heated with 10 g. of aluminium *iso*propoxide and 100 g. of *iso*propyl alcohol, at such a rate that about 20 c.c. of a mixture of acetone and *iso*propyl alcohol distilled in an hour. At the end of each hour, 20 g. of *iso*propyl alcohol were added, and after 8 hours a further 10 g. of aluminium *iso*propoxide. The process was continued for, in all, 12 hours. The mixture was cooled and decomposed with ice, and the product distilled in steam.

The distillate (2 l.) was extracted with ether, and the extract dried with sodium sulphate and freed from solvent under a column. The residue yielded 40 g. of *9-methyl-1-decalol* (probably *cis*-), b. p. 134—135°/20 mm. (Found: C, 78·3; H, 12·1. $C_{11}H_{20}O$ requires C, 78·5; H, 12·0%).

8-*Methyl*-1-*hydrindanone* (III).—A solution of 9-methyl-1-decalone (16 g.) in acetic anhydride (10 c.c.) was added in drops to 50 c.c. of concentrated nitric acid, previously heated nearly to boiling, at such a rate that the acid was kept gently boiling. Finally the mixture was boiled for 2 minutes, diluted with 20 c.c. of water, and boiled for a further 20 minutes. The product was evaporated over caustic potash in a vacuum desiccator. The acid fraction (12 g.) was separated by means of sodium bicarbonate. The neutral product (7 g.) was used for further oxidations. The gummy 2-methyl*cyclo*hexane-2-carboxylic-1-β-propionic acid would not solidify even after distillation under reduced pressure (cf. Kon, Linstead, and Simons; and Robinson and Walker, *locc. cit.*). 12 G. of the crude acid were heated with 1 g. of baryta to 270—290°, finally to 320°. The distillate was extracted with light petroleum (b. p. 50°), and the extract washed with aqueous sodium hydroxide, dried, and evaporated. The residue was treated with 12 g. of semicarbazide hydrochloride, 10 g. of sodium acetate, and sufficient methanol. The semicarbazone was not formed at 25°, but separated readily on the steam-bath, in agreement with Linstead, Millidge, and Walpole (*loc. cit.*). The yield of pure, twice crystallised semicarbazone, m. p. 223°, was 3·8 g. From this, 2·0 g. of 8-methyl-1-hydrindanone (probably *cis*-), b. p. 95—96°/12 mm., m. p. 34°, were regenerated. The ketone and the semicarbazone did not depress the m. p.'s of the corresponding products of Kon, Linstead, and Simons.

9-Methyl-1-decalol (20 g.) was added in small quantities to 50 c.c. of concentrated nitric acid, the vigour of the reaction being controlled by cooling in ice. The product was warmed on the steam-bath for 5 minutes, kept for 2 hours, and worked up as above. The acid, which did not solidify, was converted into 8-methyl-1-hydrindanone as before. The yields were 8 g. of non-acidic material and 18 g. of acid, which gave 4·8 g. of distilled solid ketone and 2 g. of uncyclised acid.

The 8-methyl-1-hydrindanone on oxidation with nitric acid in acetic anhydride yielded an acid, m. p. (crude) 152—154°, and 165° after crystallisation. A mixed m. p. with the 2-methyl-*cyclo*hexane-2-carboxylic-1-acetic acid, m. p. 164°, of Linstead and Millidge (*loc. cit.*) showed no depression.

6 G. of the 10-chloro-9-methyl-1-decalone obtained above were stirred under reflux in a bath at 95° for 3 hours with 5·2 g. of resublimed aluminium chloride and 30 c.c. of sodium-dried *cyclo*hexane, moisture being excluded (cf. Nenitzescu and Cantuniari, *loc. cit.*). The product was cooled and poured on ice and dilute acid, and the ketonic material, isolated by means of light petroleum, was distilled. The fractions boiling above 102°/13 mm. gave a little *semicarbazone* of a *9-methyl-1-octalone* which, after crystallisation from methanol, melted at 228° but greatly depressed the m. p.'s of the semicarbazone of 9-methyloctalone, obtained by means of dimethyl-aniline, and of that of 9-methyl-1-decalone (Found: C, 65·2, 65·3; H, 8·5, 8·6. $C_{12}H_{19}ON_3$ requires C, 65·1; H, 8·7%). Presumably this corresponds with a different position of the double bond.

*Cyclisation of* 2-*Methyl*-1-$\Delta^3$-n-*pentenyl*cyclo*hexanol* (IV).—70 G. of the alcohol (IV) were added to a stirred, ice-cooled mixture of 210 c.c. of glacial acetic acid, 30 c.c. of acetic anhydride, and 12 c.c. of concentrated sulphuric acid. The mixture turned dark red and remained clear, but after the addition of a further 11 c.c. of concentrated sulphuric acid, it soon became dark brown and turbid, and separated into two clear layers. The colourless upper layer almost disappeared after 12 hours' standing. After 80 hours, the product from two such cyclisations was poured into 1200 c.c. of ice-water, well shaken, and extracted with ether. The extract was washed with alkali and dried over anhydrous potassium carbonate. The solvent was removed, and the residue hydrolysed (3 hours' boiling with 50 g. of caustic potash in 250 c.c. of methanol). The neutral product was fractionated into 29 g. of hydrocarbon, b. p. 98—103°/12 mm. (25%), and 65 g. of alcohol, b. p. 143—147°/12 mm. (46%).

The hydrocarbon (? 1:9-dimethyloctalin; X) had $d_{4°}^{16·7°}$ 0·9121, $n_D^{16·7°}$ 1·4975, $[R_L]_D$ 52·63, (calc. for $|_1^{=}$, 52·75). The *alcohol* (? 1:9-dimethyl-2- or-3-decalol) had b. p. 152°/17 mm., $d_{4°}^{14·6°}$ 1·0028, $n_D^{14·6°}$ 1·5074, $[R_L]_D$ 54·01 (calc., 54·75) (Found: C, 78·9; H, 12·1. $C_{12}H_{22}O$ requires C, 79·0; H, 12·2%). It failed to solidify at − 20°.

A solution of 40 g. of the alcohol in 120 c.c. of acetic acid was treated with 15 g. of chromic acid dissolved in the minimum amount of water, and the oxidation completed in the usual manner. The ketone, isolated by extraction with light petroleum, boiled at 140—142°/14 mm. (32 g., 81%). The sparingly soluble *semicarbazone* melted crude at 216° and at 223° after three

crystallisations from methanol (Found : C, 65·2; H, 9·7. $C_{13}H_{23}ON_3$ requires C, 65·7; H, 9·8%). The pure *ketone* (? 1 : 9-dimethyl-2- or-3-decalone) regenerated from the semicarbazone had b. p. 138·5°/13 mm., $d_{4°}^{18·6°}$ 0·9910, $n_D^{18·6°}$ 1·4966, $[R_L]_D$ 53·16 (calc., 53·23) (Found : C, 79·6; H, 11·1. $C_{12}H_{20}O$ requires C, 79·9; H, 11·2%).

The alcohol (25 g.) was heated for 90 minutes with an equal weight of potassium bisulphate at 180°. Extraction of the product with ether yielded an *olefin*, $C_{12}H_{20}$ (? 1 : 9-dimethyl-$\Delta^2$-octalin; X), which was purified by heating with potassium at 170° and distillation at 95—99°/10 mm. Yield, 70%. The product had $d_{4°}^{18·4°}$ 0·9153, $n_D^{18·4°}$ 1·4974, $[R_L]_D$ 52·52 (calc. for $|_1^=$, 52·75), physical properties very close to those of the olefin obtained as a by-product in the cyclisation (Found : C, 87·5; H, 12·4. $C_{12}H_{20}$ requires C, 87·7; H, 12·3%). A similar product was obtained in 51% yield by dehydrating with oxalic acid. A solid nitrosochloride could not be obtained.

16 G. of the olefin (potassium bisulphate product) were shaken overnight with 6 g. of sodium carbonate and 1200 c.c. of 3% aqueous potassium permanganate. The product, worked up in the usual manner, yielded an acid which failed to solidify. It was esterified by means of ethereal diazomethane, and the main fraction of the ester (b. p. 130—140°/0·2 mm.) was hydrolysed with hydrochloric acid. The gum so obtained eventually solidified and the *acid* (? 1-methyl*cyclo*hexane-1-α-propionic-2-acetic acid; XI), melted at 156° after several crystallisations from water, in which it was not very soluble (Found : C, 63·1; H, 8·7. $C_{12}H_{20}O_4$ requires C, 63·1; H, 8·9%). The same acid was obtained by oxidising the ketone $C_{12}H_{20}O$ with boiling concentrated nitric acid. When the ketone (6·2 g.) was treated with chromium trioxide (4·6 g.), concentrated sulphuric acid (5 c.c.), and water (30 c.c.), there was little reaction, and no ketonic acid could be isolated from the product.

The dibasic acid $C_{12}H_{20}O_4$ (12 g. of crude gum), mixed with 0·2 g. of baryta, was converted into ketone in the manner already described for the preparation of 8-methyl-1-hydrindanone. 6 G. of crude *semicarbazone* were obtained, which after three crystallisations from methanol melted at 214·5° (Found : C, 64·35; H, 9·2. $C_{12}H_{21}ON_3$ requires C, 64·5; H, 9·5%). Ketonisation of the pure acid, m. p. 156°, gave the same compound. Regeneration from 3·2 g. of the pure semicarbazone yielded 2·0 g. of a *ketone*, $C_{11}H_{18}O$ (? 1 : 8-dimethyl-2-hydrindanone; XII), with b. p. 114°/9 mm., $d_{4°}^{18·8°}$ 0·9862, $n_D^{18·8°}$ 1·4896, $[R_L]_D$ 48·67 (calc., 48·61) (Found : C, 80·2; H, 11·0. $C_{11}H_{18}O$ requires C, 80·4; H, 11·05%).

Oxidation of the ketone with boiling nitric acid yielded an acid oil which rapidly solidified. After two crystallisations from water, white crystals of an *acid* (? 1-methyl*cyclo*hexane-1-α-propionic-2-carboxylic acid; XIII) were obtained, m. p. 144° (Found : C, 62·0; H, 8·3. $C_{11}H_{18}O_4$ requires C, 61·6; H, 8·5%). The m. p. was depressed by 2-methyl*cyclo*hexane-1 : 1-diacetic acid, m. p. 148° (Kon and Thorpe, J., 1919, **115**, 694).

*Dehydrogenation.*—(1) The olefin (1 g.) was refluxed vigorously for 3 hours in a stream of carbon dioxide over palladised charcoal. The total quantity of hydrogen evolved was less than 10 c.c., all of which came over in the first 10 minutes. The activity of the catalyst was checked against tetralin. (2) The olefin (1·2 g.) was passed over palladised asbestos, maintained at 335°, during 4 hours; 200 c.c. of gas were evolved. The product was swept out with hydrogen and converted directly into picrate with an excess of picric acid. The aromatic hydrocarbon (a liquid, 0·08 g.) was regenerated with ammonia and again converted into *picrate*. After crystallisation from methanol, this formed chrome-yellow needles, m. p. 134—135°, and gave the analysis of a dimethylnaphthalene picrate (Found : C, 56·05, 55·8; H, 4·0, 3·9. $C_{12}H_{12},C_6H_3O_7N_3$ requires C, 56·1; H, 3·9%). Admixture with the picrate of 1 : 5-dimethylnaphthalene (m. p. 137°) depressed the m. p. to 132—133°. It appears probable that the picrate is a mixture; the most likely components are the picrates of 1 : 8- and 1 : 2-dimethyl- and perhaps a little 1-methyl-naphthalene. (3) Dehydrogenation of the olefin with sulphur gave no picrate-forming material. (4) 6 G. of the ketone $C_{12}H_{20}O$ were refluxed with 0·6 g. of 30% palladised charcoal for 40 hours. The temperature fell from 260° to 220° and some water separated. A trace of phenol was separated from the product by means of caustic soda; this had m. p. 92—96°, gave a red-purple colour with ferric chloride, and formed a red picrate, m. p. 140—148°. The quantity was insufficient for complete purification, but these results are not inconsistent with the material being impure 1-methyl-2-naphthol. No picrate could be obtained from the neutral fraction.

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# 118. *Fused Carbon Rings. Part XV. Synthesis of Derivatives of 8-Methylhydrindane and of Perhydroanthracene from Substances containing a* n*-Butenyl Side Chain. Dehydrogenation of 8-Methylhydrindane.*

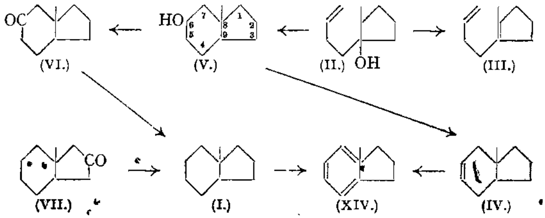
By K. D. Errington and R. P. Linstead.

The paper is mainly concerned with an extension of a synthetic method for the fusion of *cyclo*hexane rings on to alicyclic systems. The method is to introduce a *n*-$\Delta^{\gamma}$-butenyl side chain by the Grignard reaction and to cyclise the tertiary alcohol so obtained by acetic and sulphuric acids or by phosphoric acid. In this way 8-methyl-6-hydrindanol and 2-perhydroanthrol have been made from 2-methyl*cyclo*pentanone and *trans*-β-decalone respectively. The structure of 8-methyl-6-hydrindanol has been established (i) by degradation to 1-methyl*cyclo*pentane-1-carboxylic-2-acetic acid, which has been independently synthesised, together with various isomeric acids; (ii) by conversion into the known 8-methylhydrindane. The configurations of the various compounds are discussed.

Catalytic dehydrogenation of 8-methylhydrindane under suitable conditions yields hydrindene, there being no ring enlargement or migration of the methyl group. The result is of interest in connection with the dehydrogenation of sterols and similar compounds.

In previous papers of this series (Parts VII, VIII, XIII, and XIV) we have described the preparation of 8-methylhydrindane (I) and of varions of its derivatives, substituted in the five-membered ring, which were obtained by the degradation of angular-methylated derivatives of decalin. Other compounds containing the same carbon skeleton have been described by Clemo and Dickenson (J., 1935, 735), Chuang, Ma, and Tien (*Ber.*, 1935, **68,** 1946), and du Feu, McQuillin, and Robinson (J., 1937, 53). In view of the special interest attaching to this structure, which constitutes half the aetiocholane molecule, we have now studied the direct synthesis of derivatives of 8-methylhydrindane, substituted in the six-membered ring, by the "butenyl" method (Hibbit and Linstead, J., 1936, 470; cf. J., 1936, 476; 1937, 1136, 1140).

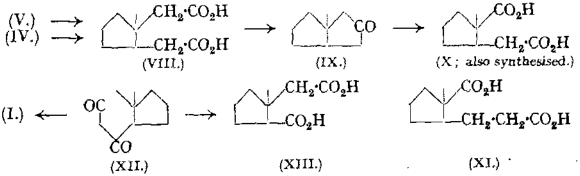
When 2-*methyl*-1-$\Delta^{\gamma}$-*butenyl*cyclo*pentanol* (II) is dehydrated by oxalic acid, it yields the corresponding *diolefin* (III), but the action of a mixture of phosphoric acid and anhydride yields the dicyclic *mono-olefin* (IV). This is also formed by similar treatment of the diene (III). If the alcohol is treated with a mixture of sulphuric acid, acetic acid, and acetic anhydride (Linstead, Millidge, and Walpole, J., 1937, 1140), the main product is the acetate of 8-*methyl*-6-*hydrindanol* (V), and hydrolysis yields the dicyclic alcohol as a crystalline solid. These reactions parallel those observed with the corresponding derivatives of *cyclo*hexane. Oxidation of the alcohol (V) with chromic acid yields the corresponding 8-methyl-6-hydrindanone (VI), which is reduced by Clemmensen's method to 8-methylhydrindane (I), identical with that obtained hy the reduction of 8-methyl-2-hydrindanone (VII) (Linstead, Millidge and Walpole, *loc. cit.*). As the hydrocarbon is a crystalline solid of m. p. 12°, the identity of the products has been established with certainty.



This evidence proves the structure of the carbon framework of the alcohol (V) and also establishes that the configuration is identical with that (probably *cis*) of 8-methyl-2-hydrindanone (VII) and the related compounds mentioned in earlier papers. It does not establish the position of the hydroxyl group. This is placed in position 6 by analogy with the syntheses of *cis*-β-decalol and of 9-methyl-2-decalol, and from the following evidence.

Oxidation of the alcohol (V) with nitric acid yields a dibasic acid $C_{10}H_{16}O_4$, m. p. 103°, and the same acid is formed by permanganate oxidation of the olefin (IV). This compound must be a 1-methyl*cyclo*pentane derivative, either the 1-carboxylic-2-β-propionic acid, the 1 : 2-diacetic acid (VIII), or the 1-β-propionic-2-carboxylic acid. Direct comparison shows that it is not identical with 1-methyl*cyclo*pentane-2 : 2-diacetic acid, which would be formed by the oxidation of a *spiro*-ketone. When heated with baryta, it yields a saturated dicyclic ketone, $C_9H_{14}O$, which must be a 7-methyl*bicyclo*[0 : 3 : 3]octanone with the keto-group in position 1, 2, or 3. Oxidation of the ketone gives an acid, $C_9H_{14}O_4$, m. p. 110°. This has been identified as 1-*methyl*cyclo*pentane*-1-*carboxylic*-2-*acetic acid* (X) by an independent synthesis, which is described later. This proves that the 7-methyl*bicyclo*-octanone is the 1- or 2- and not the 3-ketone, and hence that the parent acid, $C_{10}H_{16}O_4$, is either the *diacetic acid* (VIII) or the 1-carboxylic-2-β-propionic acid.

It is difficult to foresee the position of oxidation of an alcohol of structure (V). A. H. Cook and Linstead found that 5-hydrindanol, which contains the same ring system, was oxidised to a carboxy-propionic acid (J., 1934, 946; cf. Hückel, Goth, and Demmler, *Ber.*, **1934**, **67**, 2102). On the other hand, 9-methyl-2-decalol, which contains a similar orientation of hydroxylic and angular methyl groups, is oxidised to a diacetic acid (Linstead, Millidge, and Walpole, *loc. cit.*). It seems probable that, in the present case, the oxidation product is the diacetic acid (VIII), and hence the ketone is the 2-isomeride (IX), for the following reasons: (i) The $C_{10}$-acid is esterified with comparative ease to a neutral ester, whereas the 1-carboxyl group of the alternative structure (XI) would be expected to resist esterification. (ii) The $C_9$-ketone readily yields a semicarbazone in the cold. This parallels the behaviour of 8-methyl-2-hydrindanone, but the 1-ketone is less reactive (Linstead, Millidge, and Walpole, *loc. cit.*) and exhibits the lowered ketonic reactivity observed by Cornubert among many ketones containing two α-substituents (compare also 9-methyl-1-, -2-, and -3-decalones). This evidence is not, of course, conclusive.




To establish the identity of the final oxidation product (the acid $C_9H_{14}O_4$, m. p. 110°), we have synthesised the carboxylic-acetic acid (X) in both *cis*- and *trans*-forms. The two forms of the isomeric 1-acetic-2-carboxylic acid (XIII) had already been made by Chuang and his collaborators (*loc. cit.*) by the oxidation of 4 : 6-diketo-8-methylhydrindane (XII), first prepared by Clemo and Dickenson (*loc. cit.*). Chuang noted that the diketone was oxidised to an acid, m. p. 166°, which formed a stable anhydride, but was itself unstable, being converted by hydrochloric acid at 200° into a stereoisomeride of m. p. 101°. The second acid gave the anhydride of the acid of m. p. 166°. On these grounds Chuang assigned the *cis*-configuration to the 166° acid. Clemo and Dickenson, however, gave the *trans*-configuration to the methylhydrindane obtained by the reduction of the diketone (XII). We have confirmed the results of the Chinese workers (except that the oxidation product of the diketone melted at 169°). The 8-methylhydrindane obtained by reduction of the diketone, although not quite homogeneous, was essentially the same as that obtained by the reduction of the 8-methylhydrindanones (VI) and (VIII). We consider the *cis*-

configuration to be very probable for the diketone (XII) from Hückel's observations of the relative stabilities of *cis*- and *trans*-α-ketohydrindanes, and this to be confirmed by Chuang's evidence, which parallels the observations of A. H. Cook and Linstead (J., 1934, 956) on the corresponding unmethylated acids, the configurations of which are known with certainty. Moreover, the formation of essentially the same hydrocarbon by reduction establishes the same configuration for the diketone (XII) and the monoketones (VI and VII). The cumulative evidence that this common configuration is *cis* is now very strong.

The pair of new acids (X) was synthesised from 2-methyl*cyclo*pentanone-2-carboxylic ester. This condensed with cyanoacetic ester in the presence of piperidine, with extreme reluctance under ordinary pressure, but more readily under 4000 atmospheres (compare Newitt, Linstead, Sapiro, and Boorman, J., 1937, 879). The unsaturated *cyano-ester* so obtained, after reduction and hydrolysis, yielded one form (probably *trans*) of the acid (X), m. p. 139°. Condensation of the keto-ester with ethyl bromoacetate, followed by dehydration, catalytic reduction, and hydrolysis, yielded an isomeric acid, m. p. 110°. This was identical with that obtained by the oxidation of 7-methyl*bicyclo*octanone (IX). Barrett, A. H. Cook, and Linstead (J., 1935, 1065) obtained a form of the acid (X), m. p. 126°, by the low-pressure cyanoacetic ester route. Repetition of this showed that the product was a mixture of stereoisomerides, mainly the 139° form. As in the *cyclo*hexane series (Linstead and Millidge J., 1936, 478), the Reformatsky reaction leads to the presumed *cis*-configuration, the cyanoacetic ester route to a mixture, mainly *trans*.

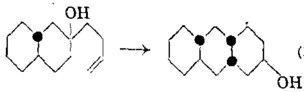
*Dehydrogenation of Hydrindane, 8-Methylhydrindane, and 8-Methylhexahydroindene*.—The dehydrogenation of 8-methylhydrindane is of obvious importance as a model for the behaviour of sterols and allied compounds. Clemo and Dickenson (*loc. cit.*) observed that the hydrocarbon was completely unaffected by dehydrogenating agents. We examined the action of the platinum and palladium catalysts used by Linstead, Millidge, Thomas, and Walpole (J., 1937, 1143) on stereochemically pure hydrocarbons made either by reducing regenerated ketones or (in the case of the olefin, IV) by dehydrating the solid alcohol (V). *trans*-Hydrindane was not dehydrogenated in the liquid phase at the boiling point over any catalyst, but in the vapour phase at 330° over platinised asbestos or palladised charcoal smoothly yielded indane (hydrindene, XIV). This agrees with Zelinsky and Titz's dehydrogenation of hydrindane (mainly *cis*, from the method of preparation) over platinised charcoal (*Ber.*, 1929, 62, 2871). *cis*-8-Methylhexahydroindene (IV) was practically unaffected over platinised asbestos at 330°, but over palladised charcoal gave indane in good yield. *cis*-8-Methylhydrindane (I) behaved in exactly the same manner. The indane was in each case identified as the 5-sulphonic acid. No indene or naphthalene was formed in any experiment, and no methylindane could be detected, although the presence of a small amount cannot be excluded.

The general conclusions are: (1) The hydrindane system is more resistant towards catalytic dehydrogenation than the decalin. (2) Only the six-membered ring is dehydrogenated. (3) Under our conditions, over the most active catalyst, the angular methyl group is eliminated: there is no migration or ring enlargement: the less vigorous platinum-black catalyst is without influence. This contrasts with the behaviour of the angular group of 9-methyldecalin and octalin, which tends to migrate to the 1-position, particularly over the milder catalyst.

The absence of migration of the angular group of 8-methylhydrindane falls into line with the experiments of J. W. Cook and Girard (*Nature*, 1934, 133, 377), Cohen, J. W. Cook, Hewett, and Girard (J., 1934, 653), and Peak and Robinson (J., 1937, 1581) on more complex compounds, and supports the general belief that the appearance of a methyl group in the five-membered ring of Diels' hydrocarbon (3'-methyl*cyclo*pentenophenanthrene) is bound up with the elimination of the long side chain.

*Synthesis of 2-Perhydroanthrol*.—We have also applied the butenyl method to the synthesis of a tricyclic compound. trans-2-$\Delta^{\gamma}$-n-*Butenyl-2-decalol* (XV) was converted into the acetate of 2-perhydroanthrol and thence into the crystalline alcohol (XVI). The ring structure is shown by the fact that dehydration, followed by dehydrogenation, gave a good yield of anthracene. From the method of synthesis and by analogy with the formation of *cis*-β-decalol from *cyclo*hexanone, the product is a *trans-cis*-compound with the

configuration shown in (XVI) (for this mode of representation, see *Chem. and Ind.*, 1937, **56**, 511).

(XV.)  (XVI.)

The formation of a hydroanthracene rather than a hydrophenanthrene derivative in this reaction provides another example of the reactivity of the 3-position in 2-decalones and similar compounds. J. W. Cook and Lawrence (J., 1937, 817), in their recent comments on this, have pointed out that both *cis*- and *trans*-compounds show this property in contrast to the sterols, where the 4-position of *cis*-3-ketones is the reactive centre in brominations and oxidations. In this respect *cis*-angular-methylated β-decalones resemble *cis*-β-decalone and not *cis*-sterol compounds such as coprostanone. Thus it has been shown (Linstead, Millidge, and Walpole, *loc. cit.*) that (*cis*-) 9-methyl-2- and -3-decalones are both oxidised at the 2—3 bond to yield 1-methyl*cyclo*hexane-1 : 2-diacetic acid in contrast to the formation of lithobilianic acid from coprostanone.

## Experimental.

*8-Methylhydrindane Group.*—Ethyl *cyclo*pentanone-2-carboxylate (Linstead and Meade, J., 1934, 935) was converted into the sodio-compound by "molecular" sodium in light petroleum and methylated with methyl iodide, unchanged material being removed with 10% alkali solution. The methylated ester (yield, 93%; b. p. 128—131°/20 mm.) gave a 65% yield of 2-methyl*cyclo*pentanone (b. p. 139—141°; semicarbazone, m. p. 182°) on hydrolysis with hydrochloric acid (1 : 1). A solution of the ketone (98 g., 1 mol.) in 200 c.c. of anhydrous ether was added in drops to the Grignard reagent prepared from 135 g. of $\Delta^{3}$-butenyl bromide (Linstead and Rydon, J., 1934, 1998). The mixture was refluxed for 2 hours and left overnight, the product decomposed with ice and ammonium chloride, and *2-methyl-1-*$\Delta^{\gamma}$*-butenyl*cyclo*pentanol* (II) isolated in the usual manner, as a colourless liquid, b. p. 87—91°/10 mm.; yield, 52 g. (35%) (Found: C, 77·7; H, 11·7. $C_{10}H_{18}O$ requires C, 77·9; H, 11·7%).

10 G. of the alcohol were heated at 150° with 15 g. of anhydrous oxalic acid for 4 hours. The product was treated with water and extracted with purified light petroleum, the extract washed with alkali and water and dried, and the solvent removed. The residue after two distillations, the second over sodium, yielded 5 g. of *2-methyl-1-*$\Delta^{\gamma}$*-butenyl*cyclo*pentene* (position of the second double bond unknown, probably as in III), a pungent-smelling liquid, b. p. 168—169°, $d_{4^\circ}^{18\cdot5^\circ}$ 0·8377, $n_D^{18\cdot5^\circ}$ 1·4665, $[R_L]_D$ 45·06 (calc. for $|\overline{2}$, 45·18) (Found: C, 88·0; H, 11·45. $C_{10}H_{16}$ requires C, 88·2; H, 11·8%). The bromine addition under the conditions of Rosenmund and Kuhnhenn was 334 and 319 g. of bromine per mole in two determinations ($2Br_2$ requires 320). 0·1264 G. of the diene in purified acetic acid over Adams's catalyst absorbed 42·8 c.c. of hydrogen at N.T.P., corresponding to 2·03 double bonds.

5 G. of the alcohol (II) were heated at 140—150° for 5 hours with 5 g. of phosphoric oxide and 25 c.c. of phosphoric acid (*d* 1·75). The product, isolated as usual, yielded a fraction, b. p. 68—74°/14 mm., which was refluxed over sodium for 30 minutes and then redistilled. 2·5 G. of *8-methylhexahydroindene* (probably IV) were obtained, b. p. 175—176°/761 mm., $d_{4^\circ}^{16\cdot5^\circ}$ 0·8879, $n_D^{16\cdot5^\circ}$ 1·4825, $[R_L]_D$ 43·69 (calc., 43·51) (Found: C, 88·1; H, 11·5. $C_{10}H_{16}$ requires C, 88·2; H, 11·8%). The olefin absorbed 168 and 173 g. of bromine per mole ($Br_2$ requires 160), and over Adams's catalyst took up hydrogen corresponding to 99% hydrogenation of one double bond. Similar treatment of the diene (III) gave a product, b. p. 176°, $d_{4^\circ}^{12\cdot5^\circ}$ 0·8854, $n_D^{12\cdot5^\circ}$ 1·4835, $[R_L]_D$ 43·90. On catalytic hydrogenation this gave a result corresponding to the presence of 1·11 double bonds. This and the physical properties indicate that the product is the cyclic monolefin (IV) contaminated with a little unchanged diene. 8-Methylhexahydroindene with very similar properties (b. p. 176°, $d_{4^\circ}^{19^\circ}$ 0·8891, $n_D^{19^\circ}$ 1·4810, $[R_L]_D$ 43·58) was also made by dehydrating pure solid 8-methyl-6-hydrindanol with potassium hydrogen sulphate.

23 G. of the alcohol (II) were slowly added at 0° to 150 c.c. of a reagent made from glacial acetic acid (200 c.c.), acetic anhydride (20 c.c.), and concentrated sulphuric acid (20 c.c.). After 5 days' standing, the mixture was worked up as described by Linstead, Wang, Williams, and Errington (J., 1937, 1136), and the crude acetate hydrolysed. Distillation of the neutral product of the hydrolysis yielded 1·8 g., b. p. 80—105°/18 mm. (mainly olefin), and 16 g., b. p.

106—116°/10 mm. The second fraction rapidly solidified to a camphor-like mass, which was drained on a porous tile and crystallised from purified light petroleum. 12 G. of pure *cis-8-methyl-6-hydrindanol* (V) were so obtained, m. p. 66° (Found: C, 77·7; H, 11·4. $C_{10}H_{18}O$ requires C, 77·9; H, 11·7%). Extraction of the tile with ether and distillation gave 3 g. of a strong-smelling liquid isomeride (mainly an epimeride), b. p. 112—113°/11 mm.

Oxidation of 6 g. of the pure solid alcohol with 3 g. of chromic acid in 20 c.c. of glacial acetic acid in the usual manner gave 4·5 g. of a ketone, b. p. 107—108°/12 mm., m. p. about 24°. This reacted rapidly in the cold with semicarbazide acetate in aqueous methyl alcohol. The *semicarbazone* of *cis*-8-methyl-6-hydrindanone crystallised from methyl alcohol in large clusters, m. p. 210° (bath preheated to 200°) (Found: C, 63·5; H, 9·1. $C_{11}H_{19}ON_3$ requires C, 63·1; H, 9·2%). The same semicarbazone was obtained from the ketone, b. p. 109°/13 mm., made by oxidising the liquid alcohol mentioned above. In neither case could an isomeric semicarbazone be detected. Regeneration from the semicarbazone yielded *cis*-8-methyl-6-hydrindanone, b. p. 109°/12 mm., m. p. 37°. Reduction of this by Clemmensen's method, followed by purification of the product by washing with concentrated sulphuric acid and refluxing over sodium, yielded *cis*-8-methylhydrindane, b. p. 69°/19 mm., m. p. 12—13°, $d_{4^\circ}^{18^\circ}$ 0·8778, $n_D^{18^\circ}$ 1·4707, $[R_L]_D$ 43·96 (calc., 43·98). This hydrocarbon was practically identical in properties with that prepared by Linstead, Millidge, and Walpole (*loc. cit.*) and did not depress its m. p.

5 G. of 8-methyl-6-hydrindanol were added slowly with occasional cooling to 10 c.c. of concentrated nitric acid. After 2 hours the solution was heated to boiling and diluted with 20 c.c. of water. Solid separated from the cooled solution and more was obtained by evaporation in a vacuum desiccator. Yield, 3 g. of crude acid, giving, after crystallisation from water, 2·2 g. of pure cis-1-*methyl*cyclo*pentane*-1 : 2-*diacetic acid** (VIII) in clusters of transparent prisms, m. p. 103°, sparingly soluble in cold water, readily in hot (Found: C, 59·6; H, 8·1; equiv., 99·6. $C_{10}H_{16}O_4$ requires C, 60·0; H, 8·1%; equiv. 100·1). The same acid was obtained by oxidation of 8-methylhexahydroindene (IV) (6 g.) with 700 c.c. of 3% potassium permanganate solution at 0°. The product was worked up as usual, acidified, and extracted six times by hand aud then continuously for 2 days. Both the hand and the constant-ether extracts yielded an oily residue, which deposited the acid (VIII), m. p. (crude) 101°, 102—103° after crystallisation. Esterification of the acid (0·3 g.) with 7 c.c. of methyl alcohol and 1 c.c. of sulphuric acid (1 hour at the b. p.) gave a neutral ester (b. p. 120—130°/3 mm.) and no appreciable amount of acid ester.

4·8 G. of the dibasic acid were heated with a crystal of baryta in a fused nitrate bath at 280—290°. Ketone distilled over at once, and was extracted from the distillate with light petroleum. The extract was washed with alkali, dried, and evaporated. *cis*-7-Methyl*bicyclo*[0 : 3 : 3]-*octanone* (probably the 2-ketone, IX) boiled at 80°/12 mm., melted at 26°, and readily gave a *semicarbazone* in the cold, m. p. 178° (from methyl alcohol) (Found: C, 62·1; H, 8·6. $C_{10}H_{17}ON_3$ requires C, 61·5; H, 8·8%). 2·5 G. of the ketone were slowly added to 20 c.c. of concentrated nitric acid; after 5 minutes, the mixture was diluted with 15 c.c. of water, boiled for 15 minutes, and left over alkali in a vacuum desiccator. cis-1-*Methyl*cyclo*pentane*-1-*carboxylic*-2-*acetic acid* (X) then separated, m. p. 100—104° (crude), 110° after two crystallisations from water (Found: C, 57·9; H, 7·7. $C_9H_{14}O_4$ requires C, 58·1; H, 7·5%). It formed prisms, sparingly soluble in cold water, readily in hot.

*Synthesis of Various Methyl* cyclo*Pentanecarboxylicacetic Acids.*—(*a*) Dr. R. H. Sapiro of this College kindly carried out for us the condensation between equimolecular quantities of ethyl 2-methyl*cyclo*pentanone-2-carboxylate and ethyl cyanoacetate in the presence of piperidine at 65° under 5000 atmospheres. The reaction yielded 20% of *ethyl 2-methyl*cyclo*pentylidene-1-cyanoacetate-2-carboxylate*, b. p. 152—158°/1 mm. (Found: C, 62·9; H, 6·9. $C_{14}H_{19}O_4N$ requires C, 63·4; H, 7·2%). This was reduced with aluminium amalgam, and the product hydrolysed, following Barrett, Cook, and Linstead (*loc. cit.*). The trans-1-*methyl*cyclo*pentane-1-carboxylic-2-acetic acid* (X) so obtained formed clusters of transparent prisms, m. p. 139° after three crystallisations from water (Found: C, 58·1; H, 7·8. $C_9H_{14}O_4$ requires C, 58·1; H, 7·5%). A similar mixture (200 g.) of ethyl cyanoacetate, the keto-ester, and piperidine (¼ mol.) which had been standing for 3 years at room temperature† yielded 5 g. of condensation product, b. p. 150—160°/2 mm. By the same series of reactions this yielded a small amount of an acid, which after several crystallisations melted at 133—134°, and at 136° in admixture with the pure acid of m. p 139° (cf. Barrett, Cook, and Linstead, *loc. cit.*).

* Possibly the isomeric 1-carboxylic-2-β-propionic acid (XI); see p. 667.

† We are indebted to Dr. J. W. Barrett for this material.

(b) Ethyl 2-methyl*cyclo*pentanone-2-carboxylate (66 g.) was condensed with bromoacetic ester (34 c.c.) and magnesium (15 g.) in benzene (60 g.). After an hour's refluxing, a further 34 c.c. of bromoacetic ester were added and the reaction was completed during 2 hours on the steam-bath. The hydroxy-ester was isolated as usual (b. p. 154°/6 mm.; yield, 56%) and dehydrated with potassium hydrogen sulphate (5 hours, at 180—200°). The unsaturated ester so obtained (18 g., b. p. 150—153°/8 mm.) was reduced in acetic acid over Adams's catalyst to *ethyl* cis-*1-methyl*cyclo*pentane-1-carboxylate-2-acetate*, b. p. 140°/5 mm. (Found: C, 64·8; H, 8·5. $C_{13}H_{22}O_4$ requires C, 64·4; H, 9·2%). Hydrolysis of this ester (10 g.) with boiling hydrochloric acid for 10 hours yielded *cis*-1-methyl*cyclo*pentane-1-carboxylic-2-acetic acid (X), which melted at 108° in the crude state and at 110° after crystallisation from water. No second acid could be isolated (Found: C, 58·0; H, 7·6; equiv., 92·7. Calc. for $C_9H_{14}O_4$: C, 58·1; H, 7·5%; equiv. 93·1). The m. p. was not depressed by the acid obtained by the oxidation of 7-methyl*bicyclo*octanone.

(c) The preparation of 1-methyl*cyclo*pentane-2-carboxylic-1-acetic acid (XIII) followed that by Chuang, Ma, and Tien (*loc. cit.*). The diketone (XII), obtained in 38% yield, m. p. 90—91° (lit., 92°), on oxidation with sodium hypobromite yielded the acid (XIII), m. p. 156—157° (crude), which formed glistening flattened prisms m. p. 169—170° after two crystallisations from water (lit., 166°). No second acid could be isolated.

3·5 G. of the diketone were reduced by Clemmensen's method, the product distilled in steam, and the hydrocarbon extracted from the distillate with light petroleum. The extract was washed with concentrated sulphuric acid until there was no further coloration of the acid, then with water and alkali, dried over calcium chloride, refluxed over sodium for ½ hour, and fractionated. 0·9 G. of *8-methylhydrindane was obtained, b. p.* 68—70°/18 *mm.*, $d_{4°}^{18·5°}$ 0·8731, $n_{4°}^{18·5°}$ 1·4688, $[R_L]_D$ 44·10 (calc., 43·98). The hydrocarbon melted at about 3° alone and at 6—8° when mixed with an equal weight of *cis*-8-methylhydrindane, m. p. 12°.

*Dehydrogenations.—Materials. trans*-Hydrindane, b. p. 159°, was made by Clemmensen reduction of *trans*-2-hydrindanone, 8-methylhydrindane, m. p. 12°, by reduction of the ketone (VI), and 8-methylhexahydroindene by dehydration of the solid alcohol (V).

*Catalysts.* Platinised asbestos and palladised charcoal were made by following Linstead, Millidge, Thomas, and Walpole's directions for "Platinum 1" and "Palladium 1" (*loc. cit.*, p. 1151). The palladium was purified before use through the diammino-dichloride by the method of Wichers (*Trans. Amer. Inst. Min. Eng.*, 1928, **76**, 602; cf. Keiser and Breed, *Amer. Chem. J.*, 1894, **16**, 20). The procedure followed that used in our previous work. Small quantities of indane (hydrindene) were identified as follows: 2 c.c. of concentrated sulphuric acid were added in drops to an equal volume of indane at 0°. After standing overnight, the product was poured into 1 c.c. of water and cooled in ice. The solid mass was drained on a porous tile and crystallised from 20% (vol.) sulphuric acid. This procedure yielded 84% of the trihydrate of indane-5-sulphonic acid, white plates, m. p. 92° (A. H. Cook and Linstead, J., 1934, 952).

(i) *trans*-Hydrindane (1·4 g.), passed over platinised asbestos at 310—320°, yielded 70% of the theoretical quantity of hydrogen that would have been lost by its conversion into indane. The product (0·9 g.) had $n_D^{16°}$ 1·5276, and on sulphonation yielded indane-5-sulphonic acid, m. p. 92°. Over palladised charcoal at 310°, *trans*-hydrindane gave 84% of the theoretical quantity of hydrogen; the dehydrogenated product had $n_D^{17°}$ 1·5401, and yielded the same sulphonic acid. When *trans*-hydrindane was refluxed in the liquid phase with palladium for 100 hours in a stream of carbon dioxide, no appreciable dehydrogenation occurred, the amount of permanent gas evolved being comparable with that from a blank experiment.

(ii) 8-Methylhydrindane (1·0 g.), passed over platinum at 330—340°, yielded only 5 c.c. of gas; the recovered hydrocarbon (0·8 g.) had the characteristic odour of the starting material and almost unchanged refractivity ($n_D^{20·5°}$ 1·4739). Over palladium at 330°, 1·2 g. of 8-methylhydrindane yielded 470 c.c. of gas (*ca.* 80%). The liquid product (1·0 g.) had $n_D^{19·5°}$ 1·5336 and on sulphonation gave pure indane-5-sulphonic acid, identified as before.

(iii) 8-Methylhexahydroindene over palladium at 330° gave 55% of the theoretical quantity of gas. The liquid product had $n_D^{18·5°}$ 1·5346, and gave a 70% yield of indane-5-sulphonic acid. Over platinum at 330°, the same hydrocarbon yielded no appreciable amount of gas and had $n_D^{19°}$ 1·4833 after passage over the catalyst as against 1·4810 before.

*Synthesis of Perhydroanthrol.*—To the Grignard reagent prepared from 105 g. of $\Delta^3$-butenyl bromide, a solution of 120 g. of *trans*-2-decalone in 250 c.c. of dry ether was added slowly; the mixture was refluxed overnight and worked up in the usual manner. 75 G. of material boiling between 122° and 150°/6 mm. were obtained, which on fractionation yielded 48 g., b. p. 134—140°/5 mm.; this solidified in ice. The solid was drained on a tile and crystallised from ether

at −15°, 25 g. of pure *trans-2-Δ^γ^-n-butenyl-2-decalol* (XV) being obtained, m. p. 39° (Found: C, 80·9; H, 11·45. $C_{14}H_{24}O$ requires C, 80·7; H, 11·6%). 24 G. of the solid alcohol were cyclised during 5 days with 200 c.c. of the acetic–sulphuric acid mixture. The product was worked up and hydrolysed in the usual manner. Distillation of the neutral product yielded 12·5 g. of material, b. p. 105—120°/2 mm., which solidified in ice and was crystallised from ether. trans-cis-2-*Perhydroanthrol* (XVI) formed glistening needles, m. p. 145° (Found: C, 80·7; H, 11·45. $C_{14}H_{24}O$ requires C, 80·7; H, 11·6%). More of the same material was obtained by a similar cyclisation of liquid portions of the butenyldecalol. During the cyclisation of 5 g. of this crude alcohol with 10 c.c. of the usual reagent, some solid separated. This crystallised from ether in stout prisms, m. p. 125—126°, showed the reactions of a ketone, and yielded a semicarbazone (needles from benzene), m. p. 210—211°. It was identified as *trans*-octahydronaphthyl-*trans*-2-decalone by mixed m. p. determinations of the ketone and semicarbazone with authentic specimens (Thakur, J., 1933, 1477) and by analysis (Found: C, 83·7; H, 10·6. Calc.: C, 83·9; H, 10·55%). This substance was presumably produced by self-condensation of decalone present as impurity in the butenyldecalol.

Dehydration of 2-perhydroanthrol with its own weight of phosphoric oxide at 140° for 1 hour yielded dodecahydroanthracene, which after 30 minutes' refluxing over sodium boiled at 112—115°/15 mm. 1·2 G. of this hydrocarbon, when passed in the vapour phase over palladised charcoal at 320°, yielded 60% of the theoretical quantity of hydrogen and 0·63 g. of a fluorescent solid, m. p. 193—198°. After sublimation this had m. p. 211°, not depressed by anthracene. It was further identified by conversion into the easily dissociated picrate and into anthraquinone.

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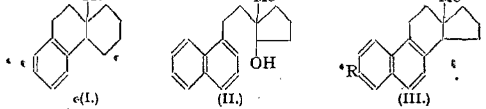
## 119. *Syntheses of Polycyclic Compounds related to the Sterols. Part VI.*

By George A. R. Kon and Eric S. Narracott.

In Part I (J., 1933, 1081) it was stated that the direct cyclodehydration of 2-methyl-2-β-phenylethyl*cyclo*hexanol gave 11-methyloctahydrophenanthrene (I), in which the angular methyl group occupies a position corresponding to $C_{13}$ of the sterols. Further work shows that the dehydration of carbinols of this type is accompanied by a retropinacolic change and the hydrocarbon produced is the 12-methyl compound, with the methyl group in a position corresponding to $C_{10}$ of the sterols. The above carbinol, the isomeric 2-methyl-1-β-phenylethyl*cyclo*hexanol, and the corresponding phenylethyl- and naphthylethyl-*cyclo*pentanols have been dehydrated to the unsaturated hydrocarbons by the xanthate method, which does not cause rearrangement; those hydrocarbons in which the methyl and the arylethyl group are on adjacent carbon atoms can be cyclised by the action of aluminium chloride, whereas the isomeric 1-methyl-1-arylethyl compounds are not cyclised. Compounds of the latter type can be cyclised by means of phosphoric oxide, but the change is accompanied by a rearrangement and hydrocarbons with an angular methyl group in a position corresponding to $C_{13}$ of the sterols cannot be obtained by this process.

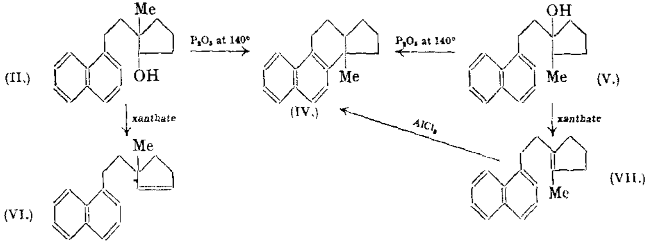
In Part I one of us (Kon, J., 1933, 1081) described the preparation of the hydrocarbon (I) by the cyclodehydration of 2-methyl-2-β-phenylethyl*cyclo*hexanol, and an analogous hydrocarbon has since been obtained in these laboratories by Dr. F. C. J. Ruzicka from the corresponding *cyclo*pentanol.




(I.) (II.) (III.)

It was hoped to employ the same method for the preparation of the tetracyclic compound (III, R = H), which was to serve as a model for the synthesis of deoxoequilenin methyl ether (III, R = OMe) or a stereoisomeride of it.

An initial difficulty arose in the preparation of the carbinol (II) from the corresponding ketone, because the reduction of the latter with sodium in moist ether gave an *alcohol* $C_{18}H_{24}O$, containing two atoms of hydrogen more than was expected. This underwent cyclodehydration, giving a *hydrocarbon* $C_{18}H_{22}$ possessing the expected skeleton, since it was smoothly dehydrogenated to *cyclo*pentenophenanthrene, but it is clear that the production of dihydronaphthalene derivatives in the reduction of naphthylethyl*cyclo*pentanones, already noted in Part I (*loc. cit.*), renders this method valueless for the synthesis of deoxoequilenin methyl ether. Trial experiments on the reduction of 2-β-naphthylethyl*cyclo*pentanone showed that Ponndorf's method could not be applied, but the desired result was ultimately achieved by using hydrogen in the presence of Adams's catalyst. The *carbinol* (II) gave on dehydration with phosphoric oxide a hydrocarbon, which was characterised by its crystalline addition *compound* with *s*-trinitrobenzene; this proved to be identical with that prepared from the cyclisation product of the isomeric carbinol (V), which must have the structure (IV) (Harper, Kon, and Ruzicka, J., 1934, 124).




It is clear that in the dehydration of one of these carbinols a retropinacolic change must have taken place. Such a change would, indeed, be expected in a carbinol of the structure (II), in which there is a quaternary carbon atom next to the carbon atom carrying the hydroxyl, even though there is a methylene group on the other side of it, which allows dehydration without rearrangement. It has been possible to show that it is the carbinol (II) and not (V) which undergoes this abnormal reaction. Both carbinols were dehydrated to the corresponding cyclo*pentenes*, (VI) and (VII) respectively, by the xanthic ester method of Tschugaev as modified by Whitmore and Simpson (*J. Amer. Chem. Soc.*, 1933, **58**, 3809); the two hydrocarbons were quite distinct and were characterised by their addition products with *s*-trinitrobenzene. The componnd (VII) was cyclised to the hydrocarbon (IV) by means of aluminium chloride (compare Cook and Hewett, J., 1933, 1098), but the isomeride (VI) could not be cyclised by any of the reagents tried and we have thus been unable to prepare the hydrocarbon (III, R = H).

The simpler hydrocarbons of the types (VI) and (VII) with a phenyl residue in place of naphthyl were similarly prepared from the isomeric *cyclo*pentanols and were found to behave in the same way. The structures of the hydrocarbons, which differ appreciably in their physical constants, have been confirmed by oxidation: the compound of the type (VII), which is most readily prepared by distilling 2-methyl-1-β-phenylethyl*cyclo*pentanol with a trace of iodine, gives a diketone on treatment with permanganate, and is easily cyclised by means of aluminium chloride to the tricyclic compound analogous to (IV), which has already been prepared by direct cyclodehydration of the parent carbinol. The isomeric hydrocarbon of type (VI) is oxidised to an acidic product by the action of permanganate; in place of the expected glutaric acid a ketonic *acid* is obtained, characterised by the formation of a *semicarbazone*. As this acid does not react with *o*-phenylenediamine or give a colour with ferric

chloride, it must be inferred that it is a $\gamma$-keto-acid formed by the oxidation of the methylene group next to the phenyl group, of the formula $Ph\cdot CO\cdot CH_2\cdot CMe(CO_2H)\cdot CH_2\cdot CH_2\cdot CO_2H$, the formation of which fully confirms the structure assigned to the parent hydrocarbon (the oxidation of phenylated side-chains in the manner assumed above is well known). All attempts to cyclise the hydrocarbon to a saturated isomeride were unsuccessful, except with the aid of phosphoric oxide; the properties of the compound formed in the latter case left little doubt that it was formed as the result of a rearrangement and was identical with the product of direct cyclodehydration of *either* isomeric carbinol. Precisely similar observations were made with the analogous *cyclo*hexane derivatives; two isomeric *cyclo*hexenes were prepared, their structures confirmed by oxidation, and cyclisation attempted. Only the compound analogous to (VII) could be converted into the hydrophenanthrene with aluminium chloride and it can be inferred that the compound previously described as (I) has in reality the alternative structure with the angular methyl group in position 12, not 11, a conclusion well supported by a comparison of the physical properties of the supposed 11-methyl compound with those of its isomeride (Kon, *loc. cit.*); it is unfortunately impossible to obtain a more conclusive proof of their identity, as the hydrocarbons are liquid and do not form solid derivatives.

## Experimental.

2-β-1'-*Naphthylethyl*cyclo*pentanone*.—This ketone was prepared as described by Kon (*loc. cit.*), but it was found that the yield is greatly influenced by the temperature at which the pyrolysis of the naphthylethyladipic acid is carried out; the highest yield (50%) is obtained at 360° and diminishes rapidly below and above this temperature with the formation of α-methylnaphthalene at the expense of the ketone. A 50% yield of the latter is, however, invariably obtained if the acid is first heated with twice its weight of acetic anhydride for 2 hours, the reagent then distilled off, and the residue slowly pyrolysed.

2-β-1'-*Naphthylethyl*cyclo*pentanol*.—5·6 G. of the ketone in 50 c.c. of ethyl alcohol were shaken in an atmosphere of hydrogen with 0·5 g. of Adams's catalyst for 7 hours; absorption then ceased. When the filtered solution was treated with semicarbazide acetate, no semicarbazone was obtained; the *alcohol* was recovered by addition of water and extraction with ether and purified in the usual way, 5 g. of a pale yellow, viscous oil being obtained, b. p. 168—174°/0·4 mm. (Found: C, 84·4; H, 8·2. $C_{17}H_{20}O$ requires C, 84·9; H, 8·4%). The 3 : 5-dinitrobenzoate formed small needles, m. p. 194—195°.

The alcohol readily undergoes cyclisation with phosphoric oxide at 140° and the resulting hydrocarbon, b. p. 108—110°/0·4 mm., gives a good yield of 1 : 2-*cyclo*pentenophenanthrene on dehydrogenation with selenium.

2-*Methyl*-2-β-1'-*naphthylethyl*cyclo*pentanone*.—The preceding ketone (22 g.) was methylated in the presence of sodamide by the method of Haller and Cornubert (*Bull. Soc. chim.*, 1931, **41**, 367) as described by Kon (*loc. cit.*), the product distilled, and the appropriate fraction converted into the *semicarbazone*. This was fractionally crystallised from alcohol and 6·5 g. of product, m. p. 209°, were obtained (Found: C, 73·8; H, 7·6. $C_{19}H_{23}ON_3$ requires C, 73·7; H, 7·5%). The *ketone* regenerated from it by means of hydrochloric acid had b. p. 182°/0·2 mm. (Found: C, 85·6; H, 7·9. $C_{18}H_{20}O$ requires C, 85·7; H, 7·9%).

*Reduction*. (1) The ketone (10·5 g.) was reduced with sodium in moist ether (compare Bardhan and Sen-Gupta, J., 1932, 2520) and gave 8·5 g. of an *alcohol*, b. p. 194°/1 mm., together with a little unchanged ketone, which was recovered as the semicarbazone. The alcohol was the dihydro-derivative of the expected compound (Found: C, 83·9; H, 9·1. $C_{18}H_{24}O$ requires C, 84·3; H, 9·5%); it formed a 3 : 5-dinitrobenzoate, m. p. 170°, and gave on cyclisation with phosphoric oxide at 140° a *hydrocarbon*, b. p. 159—170°/0·2 mm. (Found: C, 90·6; H, 9·3. $C_{18}H_{22}$ requires C, 90·7; H, 9·3%), which gave 1 : 2-*cyclo*pentenophenanthrene on dehydrogenation with selenium.

(2) The ketone was catalytically reduced as described above, giving a quantitative yield of 2-*methyl*-2-β-1'-*naphthylethyl*cyclo*pentanol* (II), b. p. 214—220°/1 mm.; this solidified to a greasy mass, m. p. 69—71°, which could not be recrystallised (Found: C, 85·3; H, 9·0. $C_{18}H_{22}O$ requires C, 85·0; H, 8·7%), and formed a 3 : 5-dinitrobenzoate, m. p. 186°.

*Cyclodehydration*. 2·5 G. of the carbinol (II) were heated with 5 g. of phosphoric oxide for 1 hour at 140°. The hydrocarbon (IV) (1·7 g.), isolated after addition of ice and extraction with ether, was a colourless oil with a blue fluorescence, b.p. 208—212°/3 mm., which did not decolorise

bromine in chloroform (Found: C, 91·5; H, 8·6. Calc. for $C_{18}H_{20}$: C, 91·5; H, 8·5%). It formed an unstable orange-yellow picrate, m. p. 71—72°, and the s-*trinitrobenzene* complex crystallised from alcohol in fine needles, m. p. 103—103·5°, not depressed by the compound, m. p. 104°, described below (Found: C, 63·7; H, 5·3. $C_{18}H_{20},C_6H_3O_6N_3$ requires C, 64·1; H, 5·2%). The hydrocarbon was dehydrogenated by heating with half its weight of selenium for 22 hours at 310° and gave 1 : 2-*cyclo*pentenophenanthrene.

*2-Methyl-2-β-1'-naphthylethyl-Δ⁵-*cyclo*pentene* (VI).—4·5 G. of the carbinol (II) in 50 c.c. of ether were added to 1 g. of potassium hydroxide, 50 c.c. of carbon tetrachloride, and 30 c.c. of ether; the mixture was mechanically stirred for an hour, and 1·1 c.c. of carbon disulphide then added. After a further 8 hours' stirring, 1·2 c.c. of methyl iodide were added, and the mixture heated under reflux overnight. After removal of the potassium iodide the filtrate was distilled, finally in a high vacuum; 3·7 g. of the unsaturated *hydrocarbon* (VI), b. p. 168—172°/0·5 mm., were then collected (Found: C, 91·4; H, 8·5. $C_{18}H_{20}$ requires C, 91·5; H, 8·5%). The *s*-trinitrobenzene complex crystallised from alcohol in pale yellow needles, m. p. 102·5—103°; it was more soluble and paler in colour than that of the cyclic isomeride (IV), but did not depress its m. p.

*2-Methyl-1-β-1'-naphthylethyl-Δ¹-*cyclo*pentene* (VII).—2-Methyl-1-β-1'-naphthylethyl*cyclo*pentanol (Harper, Kon, and Ruzicka, *loc. cit.*) was very readily dehydrated; distillation with a trace of iodine gave an excellent yield of the unsaturated *hydrocarbon* (VII), b. p. 132—140°/0·2 mm., which, like its isomeride (VI), decolorised bromine in chloroform (Found: C, 91·4; H, 8·5. $C_{18}H_{20}$ requires C, 91·5; H, 8·5%). The s-*trinitrobenzene* complex formed pale yellow needles, m. p. 85°, from alcohol (Found: C, 64·2; H, 5·0. $C_{18}H_{20},C_6H_3O_6N_3$ requires C, 64·1; H, 5·2%).

*Cyclisation.* 2 G. of the hydrocarbon (VII) in 20 c.c. of carbon disulphide were treated at 0° with 2·7 g. of powdered aluminium chloride in several portions, then kept overnight at 0°. After addition of ice and hydrochloric acid, the hydrocarbon (IV) was extracted with ether, 1 g., b. p. 160—165°/0·5 mm., being obtained as a colourless oil saturated to bromine. The *s*-trinitrobenzene complex formed deep yellow needles, m. p. 104°, from alcohol (Found: C, 63·7; H, 5·3. Calc.: C, 64·1; H, 5·2%). The hydrocarbon regenerated from the complex was still a viscous oil, $d_4^{19.4°}$ 1·0692, $n_D$ 1·6176. It is most readily obtained by the direct cyclodehydration of the carbinol (V).

*2-Methyl-2-β-phenylethyl*cyclo*pentanone.*—54 G. of 2-β-phenylethyl*cyclo*pentanone (Kon, *loc. cit.*) were methylated with sodamide and methyl iodide by the method used for the corresponding *cyclo*hexanone (*loc. cit.*), 40 g. of a fraction, b. p. 135—140°/1 mm., being obtained; this was converted into the *semicarbazone*, which, repeatedly crystallised from methyl alcohol, in which it was appreciably more soluble than the semicarbazone of the parent compound, formed small prisms, m. p. 191—192° (Found: C, 69·5; H, 8·5. $C_{15}H_{21}ON_3$ requires C, 69·3; H, 8·2%). The *ketone* regenerated from it had b. p. 136—137°/1 mm., $d_4^{19.3°}$ 1·0064, $n_D$ 1·52480, $[R_L]_D$ 61·53 (Found: C, 82·9; H, 9·2. $C_{14}H_{18}O$ requires C, 83·1; H, 9·0%).

*2-Methyl-2-β-phenylethyl*cyclo*pentanol.*—Reduction of the ketone with sodium in moist ether gave an almost quantitative yield of the *alcohol*, b. p. 161°/3 mm. (Found: C, 82·3; H, 9·8. $C_{14}H_{20}O$ requires C, 82·2; H, 9·9%).

*Cyclodehydration.** Treatment of the alcohol (16 g.) with phosphoric oxide as described on p. 674 gave 12 g. of a hydrocarbon, b. p. 134°/13 mm. This was shaken in petroleum solution with successive small quantities of sulphuric acid until the latter was no longer coloured. The hydrocarbon thus freed from a small amount of unsaturated material had b. p. 125—126°/11 mm., $d_4^{16.0°}$ 0·99575, $n_D$ 1·5480, $[R_L]_D$ 59·37, properties very close to those recorded for 1-methyl-1 : 2-*cyclo*pentano-1 : 2 : 3 : 4-tetrahydronaphthalene (Kon, *loc. cit.*).

*2-Methyl-2-β-phenylethyl-Δ⁵-*cyclo*pentene.*—In this and subsequent preparations Tschugaev's original method was adopted, as Whitmore and Simpson's procedure gave a poor yield of unsaturated hydrocarbon. 10 G. of the alcohol were boiled overnight with 2 g. of potassium in 70 c.c. of benzene, 5 c.c. of carbon disulphide added with 50 c.c. of ether, and the mixture boiled for 8 hours, then again overnight after addition of 5 c.c. of methyl iodide. The cooled solution was filtered, the solvent distilled, and the residue slowly distilled under reduced pressure. The crude distillate was shaken in ethereal solution with 20% aqueous potassium hydroxide, then with a saturated solution of mercuric chloride until no further precipitation of mercury salts took place. After drying, and distillation of the solvent, the residue was distilled and finally redistilled over sodium, 7 g. of the *hydrocarbon*, b. p. 142°/23 mm., being obtained,

* For this and the two preceding preparations we are indebted to Dr. F. C. J. Ruzicka.

$d_{4°}^{16\cdot3°}$ 0·93055, $n_D$ 1·52148, $[R_L]_D$ 60·30 (Found : C, 90·5; H, 9·5. $C_{14}H_{18}$ requires C, 90·3; H, 9·7%).

*Oxidation.* 2 G. of the above hydrocarbon were shaken overnight with the theoretical amount of 3% potassium permanganate solution; as the colour of the reagent had disappeared, a further amount was added, and the shaking continued until the colour persisted. The excess of reagent was destroyed with sulphur dioxide, and the product extracted with ether and shaken with alkali. No neutral products had been formed; acidification of the alkaline extract gave, on evaporation of the solution, an *acid* which crystallised from water in needles, m. p. 184° (Found : C, 63·6; H, 6·1. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·1%). This formed a *semicarbazone*, m. p. 183° (Found : C, 56·2; H, 5·9. $C_{15}H_{19}O_5N_3$ requires C, 56·1; H, 6·0%).

*2-Methyl-1-β-phenylethyl*cyclo*pentanol.*—A Grignard reagent prepared from 45 g. of β-phenylethyl bromide in 500 c.c. of ether was gradually treated with 24 g. of 2-methyl*cyclo*pentanone in the cold, and the mixture then warmed for ½ hour; 16 g. of the carbinol, b. p. 154—156°/20 mm., were ultimately obtained.

*2-Methyl-1-β-phenylethyl-Δ¹-*cyclo*pentene.*—This compound has already been obtained by the accidental dehydration of 1-methyl-2-β-phenylethyl*cyclo*pentanol (Kon, *loc. cit.*). A specimen prepared from the above carbinol by distillation with a trace of iodine had b. p. 143—144°/22 mm., $d_{4°}^{18\cdot5°}$ 0·93644, $n_D$ 1·52523, $[R_L]_D$ 60·93 (Found : C, 89·7; H, 9·6. Calc. for $C_{14}H_{18}$ : C, 90·3; H, 9·7%). A specimen obtained by the xanthate method had $d_{4°}^{20\cdot3°}$ 0·93747, $n_D$ 1·52391.

*Oxidation.* The hydrocarbon was oxidised as described above ; no acidic material was produced. When the neutral portion was treated with semicarbazide acetate, a *disemicarbazone*, needles, m. p. 191—192°, from alcohol, was formed (Found : C, 58·0; H, 7·4. $C_{16}H_{24}O_2N_6$ requires C, 58·0; H, 7·3%).

*Cyclisation.* 2 G. of the hydrocarbon were cyclised as described on p. 675, giving 1·2 g. of the cyclic hydrocarbon, b. p. 140—141°/19 mm., $d_{4°}^{18\cdot5°}$ 0·99141, $n_D$ 1·54468, $[R_L]_D$ 59·18. A hydrocarbon of very similar properties was also obtained by the action of phosphoric oxide at 140° on the *cyclo*pentene, and by direct cyclodehydration (Kon, *loc. cit.*).

*2-Methyl-2-β-phenylethyl-Δ⁶-*cyclo*hexene.*—10 G. of 2-methyl-2-β-phenylethyl*cyclo*hexanol (Kon, *loc. cit.*) gave, on dehydration by the method given on p. 675, 5·6 g. of the *hydrocarbon*, b. p. 152—153°/20 mm., $d_{4°}^{17\cdot6°}$ 0·93492, $n_D$ 1·52695, $[R_L]_D$ 65·81 (Fonnd : C, 89·8; H, 10·0. $C_{15}H_{20}$ requires C, 89·9; H, 10·1%). On oxidation this compound gave no neutral products; the acidic product has not yet been obtained crystalline and is still under investigation.

*2-Methyl-1-β-phenylethyl*cyclo*hexanol.*—This *alcohol* was prepared from 2-methyl*cyclo*hexanone and β-phenylethylmagnesium bromide as described above, the yield of the fraction, b. p. 168—175°/17 mm., being 21 g. from 30 g. of the bromide; the alcohol is always contaminated by αδ-diphenylbutane, which accounts for the high percentage of carbon found on analysis (Found : C, 85·3, 85·3; H, 9·7, 9·5. $C_{15}H_{22}O$ requires C, 82·7; H, 9·9%).

*2-Methyl-1-β-phenylethyl-Δ¹-*cyclo*hexene.*—Dehydration of the above alcohol with a trace of iodine gave the unsaturated *hydrocarbon*, b. p. 153—154°/14 mm., $d_{4°}^{19\cdot4°}$ 0·95142, $n_D$ 1·53617, $[R_L]_D$ 65·61 (Found : C, 90·2; H, 10·1. $C_{15}H_{20}$ requires C, 89·9; H, 10·1%). Dehydration by the xanthate method gave a very similar product (6 g. from 10 g. of the carbinol), b. p. 161—163°/23 mm., $d_{4°}^{19\cdot4°}$ 0·95644, $n_D$ 1·53804.

*Oxidation.* After treatment with potassium permanganate as described above no acidic products were isolated; when the neutral product was treated with semicarbazide acetate, a *disemicarbazone*, m. p. 175°, was obtained; the figures obtained on analysis suggest that this still contained some compound richer in carbon, such as the semicarbazone of an unsaturated ketone formed by loss of water from the 1 : 5-diketone originally formed (Found : C, 60·2, 60·1; H, 7·4, 7·3. $C_{17}H_{26}O_2N_6$ requires C, 58·9; H, 7·6%).

*Cyclisation.* Treatment of the *cyclo*hexene (3 g.) with aluminium chloride as described on p. 675 gave 2·1 g. of the saturated hydrocarbon, b. p. 162—163°/18 mm., $d_{4°}^{17\cdot8°}$ 1·0053, $n_D$ 1·55403, in good agreement with the constants given in Part I (*loc. cit.*) for 12-methyl-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrene.

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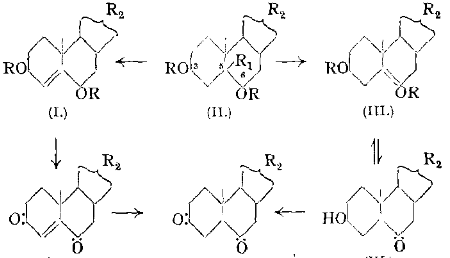
# 120. *Steroids and Related Compounds. Part II. The Dehydration of Cholestanetriol.*

By V. A. Petrow, O. Rosenheim, and W. W. Starling.

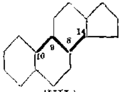
An unsaturated diol $C_{27}H_{46}O_2$ has been obtained by a Darzens dehydration of cholestane-3 : 5 : 6-triol diacetate, and its constitution as a $\Delta^4$-cholestene-3 : 6-diol established. This constitution had previously been assigned to two isomeric diols of the same empirical composition (to be referred to as Lettré's and Westphalen's diol) which were obtained from the triol by different methods. It is now shown that Lettré's unsaturated diol $C_{27}H_{46}O_2$ is a saturated keto-alcohol identical with 6-ketocholestanol, $C_{27}H_{46}O_2$. Evidence in favour of the constitution of Westphalen's diol as 5-methyl-$\Delta^{8:9}$-norcholestene-3 : 6-diol has been obtained and it is concluded that only one of the four possible stereoisomerides of $\Delta^4$-cholestene-3 : 6-diol is obtainable by the dehydration of cholestane-3 : 5 : 6-triol.

When attempting to enforce acetylation of the tertiary hydroxyl of cholestane-3 : 5 : 6-triol diacetate (II; R = Ac, $R_1$ = OH) by treatment with acetic anhydride and sulphuric acid, Westphalen (*Ber.*, 1915, **48**, 1064; cf. Dunn, Heilbron, Phipers, Samant, and Spring, J., 1934, 1580) obtained the diacetate of an unsaturated diol $C_{27}H_{46}O_2$, to be referred to as Westphalen's diol. Lettré and Inhoffen ("Über Sterine u.s.w.," 1936, p. 33; cf. Petrow, J., 1937, 1077) ascribed to this diol the constitution of a $\Delta^4$-cholestene-3 : 6-diol (I, R = H). Lettré and Müller (*Ber.*, 1937, **70**, 1947) were forced, however, to discard this view when




(I.) (II.) (III.) (IV.) (V.) (VI.)

($R_2 = C_{10}H_{30}$)




(VII.)

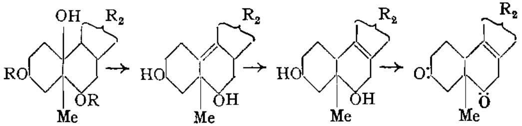
they found that on oxidation (at 4°) the diol did not yield the expected unsaturated diketone (IV), but a substance $C_{27}H_{46}O_3$ (?), m. p. 143°, which was not further characterised. They suggested that the diol might possibly have the constitution (IX).

We have now obtained, on oxidation at room temperature, an unsaturated diketone $C_{27}H_{46}O_2$, m. p. 106°, which was characterised by a *bis-2 : 4-dinitrophenylhydrazone*, m. p. 218°, and a *mono-o-tolylsemicarbazone*, m. p. 235°. Of the possible constitutions of the diketone, we favour (XI), *5-methyl-$\Delta^{8:9}$-norcholestene-3 : 6-dione*, on the assumption that the positions of the functional groups are identical in the diketone and the diol. The evidence for the proposed constitutional formula is based on the following facts: (1) Westphalen's diol is not precipitated by digitonin, showing that the spatial position of the angular methyl group at $C_{10}$ relative to the hydroxyl at $C_3$ has undergone a change during dehydration (cf. the non-precipitability of lumisterol, Dimroth, *Ber.*, 1936, **69**, 1123). This conclusion was strengthened when it was found that (2) the diol and its esters are strongly dextrorotatory: an increase of dextrorotatory power is known to follow changes in the relative position of the 10-methyl and the 3-hydroxyl group (cf. Callow and Young, *Proc. Roy. Soc.*, 1936, *A*, **890**, 194). Further, (3) the diol and its esters gave a typical green

*Tortelli–Jaffé reaction with bromine (Häussler and Brauchli, Helv. Chim. Acta,* **1929**, *12, 187), which is specific for ergosterol and steroids of analogous constitution. The ethylenic linkage of the diol may therefore be assumed to occupy a position between two quaternary carbon atoms in the ring system* ($C_8$:$C_9$ *or* $C_9$:$C_{10}$ *in VII) analogous to that of the ethylenic* linkage $C_8$:$C_{14}$ in α-ergostenol, which is responsible for the Tortelli–Jaffé reaction (cf. Heilbron and Spring, *Biochem. J.*, 1930, **24**, 133). The diol also reacts readily with selenium dioxide in alcoholic solution, a characteristic of α-ergostenol, ergosterol and other steroids which give the Tortelli–Jaffé reaction (cf. Callow and Rosenheim, J., 1933, 387).

These observations lead to the conclusion that on dehydration a structural rearrangement, hitherto unrecorded, has occurred in the steroid molecule: the typical pinacol-alcoholic group OH>C—C<CH$_3$ (5, 10) present in cholestanetriol has undergone a retro-pinacolic rearrangement, as suggested by Lettré and Müller (*loc. cit.*), leading *via* (VIII) and (IX) to 5-methyl-$\Delta^{8:9}$-norcholestene-3 : 6-diol (X) and, on oxidation of this, to the diketone (XI). The migration of the ethylenic linkage $C_9$:$C_{10}$ to $C_8$:$C_9$ during the reaction is assumed in analogy to that of $\Delta^{1:9}$-octalin to $\Delta^{9:10}$-octalin (Hückel and co-workers, *Annalen*, 1929, **474**, 121). Further, the $C_8$:$C_9$ linkage of the diol is resistant to catalytic hydrogenation, like the analogous linkage of hexadecahydrochrysene (Braun and Irmisch, *Ber.*, 1932, **65**, 883), and the diol in chloroform solution is not isomerised by treatment with hydrogen chloride.

(II, $R_1$ = OH) →




(VIII.) (IX.) (X.) (XI.)

The constitution of a $\Delta^4$-cholestene-3 : 6-diol (I, R = H) was retained, however, by Lettré and Müller (*loc. cit.*) for a substance $C_{27}H_{46}O_2$, m. p. 137—138° (to be referred to as Lettré's diol), which was obtained as a dibenzoate by pyrolysis of 5-chlorocholestane-3 : 6-diol dibenzoate (II; R = COPh, $R_1$ = Cl). The latter dibenzoate was prepared by benzoylating the chlorohydrin of cholestane-3 : 5 : 6-triol (II, R = H, $R_1$ = Cl) (Windaus, *Z. physiol. Chem.*, 1921, **117**, 155). The new diol gave, according to the above authors, a violet Liebermann–Burchard reaction, presumably taken as evidence of unsaturation, but yielded on oxidation, somewhat unexpectedly, the saturated diketone (V) instead of the unsaturated $\Delta^4$-cholestene-3 : 6-dione (IV).

We have confirmed the experimental results of the German authors, but are unable, on the following evidence, to accept their formulation of the substance $C_{27}H_{46}O_2$, m. p. 137—138°, as an unsaturated diol. Instead of the dibenzoate, m. p. 179°, from which it was derived, the " diol " yielded a monobenzoate, $C_{34}H_{50}O_3$, m. p. 179—180°, when treated in pyridine solution with benzoyl chloride in excess. A mixture of the two benzoates showed a depression of 25—30° in melting point. A monoacetate, $C_{29}H_{48}O_3$, m. p. 129—130°, resulted on acetylation. That the second oxygen atom of these esters functions as a carbonyl follows from the preparation of an acetoxy-*p*-nitrophenylhydrazone, m. p. 146—147°. Further, the " diol " $C_{27}H_{46}O_2$ yielded an *o-tolylsemicarbazone* and a *p*-nitrophenylhydrazone and was thus characterised as a keto-alcohol. The $C_6$ position of the new carbonyl group was the most likely one, and a comparison of the keto-alcohol and its derivatives with 6-ketocholestanol (Mauthner and Suida, *Monatsh.*, 1903, **24**, 654; Windaus, *Ber.*, 1903, **36**, 3755) proved their identity.

These results show that preferential elimination of chlorine at $C_5$ with hydrogen at $C_6$, rather than at $C_4$, has occurred in the pyrolysis of 5-chlorocholestane-3 : 6-diol dibenzoate, dehalogenation leading to an enol-benzoate, $\Delta^5$-cholestene-3 : 6-diol dibenzoate (III, R = COPh). In confirmation of this interpretation of the reaction, it was found that the enol-benzoate is easily obtainable, in excellent yield, by refluxing 6-ketocholestanol with

benzoyl chloride in the presence of benzoic anhydride. The enol-benzoate yields on hydrolysis the keto-alcohol (VI), which is readily oxidised to cholestane-3 : 6-dione (V) (Windaus, *loc. cit.*; Lettré and Müller, *loc. cit.*).

The atypical violet Liebermann–Burchard reaction of the saturated keto-alcohol $C_{27}H_{46}O_2$ is clearly due to its ready enolisation, introducing the ethylenic linkage $C_5$:$C_6$, which is also demonstrable by the yellow colour reaction with tetranitromethane. It was further found that all the saturated steroid ketones examined which contain a carbonyl group at $C_6$ gave a positive Liebermann–Burchard reaction (see Experimental).

It is thus proved that neither dehydration with sulphuric acid nor dehalogenation *via* the chlorohydrin gives rise to the formation of the expected $\Delta^4$-cholestene-3 : 6-diol from cholestane-3 : 5 : 6-triol. The desired diol is easily obtained, however, in quantitative yield by dehydration of the di-esters of the triol with thionyl chloride in pyridine by Darzens' method (*Compt. rend.*, 1911, **152**, 601). The resulting esters yield on hydrolysis an unsaturated diol, $C_{27}H_{46}O_2$, m. p. 256—258°. Its constitution as a $\Delta^4$-cholestene-3 : 6-diol (I, R = H) was proved by oxidation to $\Delta^4$-cholestene-3 : 6-dione (IV), which was converted into the characteristic enol-ether by mineral acids in alcoholic solution. On reduction of the diol with platinum oxide, cholestane-3 : 6-diol was obtained, which yielded cholestane-3 : 6-dione (V) on oxidation.

$\Delta^4$-Cholestene-3 : 6-diol so obtained was found to be identical with the diol, m. p. 258°, previously prepared from cholesteryl acetate by oxidation with selenium dioxide (Rosenheim and Starling, J., 1937, 377; cf. Butenandt and Hausmann, *Ber.*, 1937, **70**, 1154). Its alternative formation by the dehydration of cholestanetriol provides conclusive evidence for the interpretation of the selenium dioxide reaction, suggested by Butenandt and Hausmann (*loc. cit.*): the primary oxidation product, *i.e.*, $\Delta^5$-cholestene-3 : 4-diol, undergoes in the course of the reaction an allylic rearrangement to $\Delta^4$-cholestene-3 : 6-diol. That this allylic isomerisation is a reversible one follows from the observation that dilute mineral acids readily convert the diol, m. p. 258°, into cholestenone, in the same way as the isomeric *cis*-$\Delta^5$-cholestene-3 : 4-diol (Rosenheim and Starling, *loc. cit.*).

The interesting fact emerges from these results that the tertiary hydroxyl of cholestane-3 : 5 : 6-triol possesses an unexpected mobility, giving rise under different conditions to three isomerides $C_{27}H_{46}O_2$, of which only one is a $\Delta^4$-cholestene-3 : 6-diol.

## EXPERIMENTAL.

*Dehydration of Cholestane-3 : 5 : 6-triol with Thionyl Chloride.*—(*a*) To a solution of the cholestanetriol diacetate (2 g.) (Pickard and Yates, J., 1908, **93**, 1681) in anhydrous pyridine (10 c.c.), cooled in ice, thionyl chloride (0·4 c.c.) was added dropwise with shaking. The solution turned yellow and a white solid was formed, which was transferred into water after 5 minutes. After some hours the solid (1·8 g., m. p. 133—134°) was removed and washed with methyl alcohol. On crystallisation from methyl alcohol, colourless needles of $\Delta^4$-cholestene-3 : 6-diol diacetate (I, R = Ac) were obtained, m. p. 135—136°, $[\alpha]_D^{19°}$ − 13·2° (*c*, 1·104 *) (Found: † C, 76·7; H, 10·3. Calc. for $C_{31}H_{50}O_4$: C, 76·5; H, 10·4%).

(*b*) $\Delta^4$-Cholestene-3 : 6-diol 3-benzoate 6-acetate was obtained by the above procedure from 5-hydroxy-3-benzoyloxy-6-acetoxycholestane (5 g.) (Petrow, *loc. cit.*). The product, m. p. 127°, yielded, after crystallisation from spirit, prisms of the mixed ester, m. p. 128—129°, $[\alpha]_D^{20°}$ − 20·0° (*c*, 2·68) (Found: C, 78·6; H, 9·3. Calc. for $C_{36}H_{52}O_4$: C, 78·7; H, 9·6%).

On hydrolysis of the above esters with 5% methyl-alcoholic sodium methoxide $\Delta^4$-cholestene-3 : 6-*diol* (I, R = H) was obtained, m. p. 257—258°, $[\alpha]_D^{20°}$ + 9·0° (*c*, 1·05 in pyridine) (Found: C, 80·5; H, 11·3. Calc. for $C_{27}H_{46}O_2$: C, 80·5; H, 11·5%). On benzoylation in pyridine the diol gave the dibenzoate, m. p. 180—181°, $[\alpha]_D^{20°}$ − 73·0° (*c*, 2·62).

The diol and its esters were identical (mixed m. p.'s, optical activity) with the diol, m. p. 258°, and its esters obtained by oxidation of cholesteryl acetate with selenium dioxide (Rosenheim and Starling, *loc. cit.*). The diol gave the typical blue colour reaction with trichloroacetic acid and the Lifschütz "oxycholesterol" reaction (*Ber.*, 1908, **41**, 252) with sulphuric acid in acetic acid solution. On warming with dilute mineral acids the diol was converted into cholestenone, identified as the 2 : 4-dinitrophenylhydrazone, m. p. 233—234°.

* The optical rotations were measured in a 4 dm. tube in chloroform solution.

† Micro-analyses by Dr. G. Weiler, Oxford.

*$\Delta^4$-Cholestene-3 : 6-dione (IV).*—Kiliani's chromic acid mixture (12 c.c.) was added dropwise with mechanical stirring during 1½ hours to a suspension of the finely powdered diol (2 g.) in benzene (40 c.c.) and acetic acid (10 c.c.), and the stirring continued for a further 30 minutes. The benzene layer was separated, washed with water and dilute alkali solution, and dried over sodium sulphate. After removal of the solvent, the residue was rubbed with petrol. The insoluble colourless crystals, m. p. 122°, yielded, after recrystallisation from 85% alcohol, $\Delta^4$-cholestene-3 : 6-dione, m. p. and mixed m. p. 122—123° (Found: C, 81·6; H, 10·6. Calc. for $C_{27}H_{42}O_2$: C, 81·3; H, 10·6%). When the unsaturated dione was refluxed with alcohol containing 4% of sulphuric acid, it yielded the enol-ether $C_{29}H_{46}O_2$, m. p. and mixed m. p. 165—166°.

*$\Delta^4$-Cholestane-3 : 6-dione* (V).—The unsaturated diol (I, R = H) was catalytically reduced with platinum oxide (Rosenheim and Starling, *loc. cit.*). The product (38 mg.), m. p. 194—195°, was dissolved in acetic acid (0·5 c.c.) and oxidised with Kiliani's chromic acid mixture (0·12 c.c.). A few drops of alcohol were added to remove the excess of chromic acid, and the crystals, m. p. 168°, removed. On recrystallisation from methyl alcohol, needles of cholestane-3 : 6-dione (24 mg.), m. p. 169—170°, were obtained. The same substance resulted when $\Delta^4$-cholestene-3 : 6-dione (IV) (0·1 g.) was reduced with zinc dust (0·1 g.) in acetic acid (2·5 c.c.). A mixture of the two substances with an authentic specimen melted at 169—170°.

*Dehydration of Cholestane-3 : 5 : 6-triol with Sulphuric Acid.*—The optical activity of Westphalen's diol and its esters is given in the following table:

| | $[\alpha]_D^{18°}$. | $[\alpha]_{5461}^{18°}$. | *c*. | $\alpha_{5461}/\alpha_D$. |
|---|---|---|---|---|
| Westphalen's diol ...... | + 118·8° | + 143·6° | 1·104 | 1·21 |
| Diacetate ............... | + 83·9 | + 99·0 | 1·040 | 1·18 |
| Dibenzoate ........... | + 109·4 | + 132·9 | 1·034 | 1·22 |

A solution of the diol in 96% alcohol, to which an excess of a 1% digitonin solution in 90% alcohol had been added, was heated on a steam-bath. The solution remained clear and no precipitate was produced on keeping at 0° for 24 hours and at room temperature for 7 days.

Bromine titration (by the pyridine sulphate dibromide method) indicated that substitution as well as addition of bromine occurred. After 1, 5, and 10 minutes at room temperature, 0·050 g. of the diol absorbed 40·8, 49·5, and 50·4 mg. of bromine, corresponding to 4·1, 4·9, and 5 atoms of bromine.

The Tortelli–Jaffé reaction, carried out by adding a 1% solution of bromine in acetic acid dropwise to a chloroform solution of the diol, gave an intense green colour. The sensitivity of the reaction was increased when bromine–acetic acid containing hydrobromic acid was used, a violet-blue colour (band at 5400—5800 A.) being at first produced, which changed to green on further addition of the reagent.

In a perbenzoic acid titration, after 24 hours at 0°, 0·500 g. of the diol consumed the equivalent of 18·1 mg. of oxygen, corresponding to 1·1 ethylenic linkages.

A solution of the diol diacetate (0·5 g.) in alcohol (10 c.c.) and acetic acid (10 c.c.) was shaken with palladised charcoal (0·25 g.) in hydrogen at room temperature for 3 hours No absorption of hydrogen occurred and the diol was recovered unchanged (mixed m. p.).

*5-Methyl-$\Delta^{8:9}$-norcholestene-3 : 6-dione* (XI).—A solution of the diol (1 g.) was shaken for 6 hours at room temperature with a solution of chromic acid (0·66 g.) in water (7 c.c.) and acetic acid (15 c.c.). The neutral fraction of the oxidation products was obtained by the usual technique; it crystallised from acetone–methyl alcohol in prismatic needles, m. p. 105—106°, $[\alpha]_D^{19°}$ − 45·7° (*c*, 0·952) (Found: C, 81·0; H, 10·3. $C_{27}H_{42}O_2$ reqnires C, 81·3; H, 10·6%). The Zerewitinoff value was nil. The *diketone* gave a yellow colour with tetranitromethane and showed no absorption above 2300 A. in 0·01% alcoholic solution. The *bis*-2 : 4-*dinitrophenylhydrazone*, prepared by warming a solution of the diketone (50 mg.) and 2 : 4-dinitrophenylhydrazine (40 mg.) in alcohol (8 c.c., containing 2 drops of concentrated hydrochloric acid) on a steam-bath until a voluminous yellow precipitate formed, separated from chloroform–alcohol in yellow micro-needles, m. p. 217—218° (Found: N, 14·2. $C_{39}H_{50}O_8N_8$ requires N, 14·4%). The *mono-o-tolylsemicarbazone* was obtained by warming a solution of the diketone (50 mg.) in alcohol (1 c.c.) with a solution of *o*-tolylsemicarbazide in alcohol (5 c.c., containing 2 drops of acetic acid) on a steam-bath. Colourless clusters of needles formed after 20 minutes, and the quantity increased on cooling. The semicarbazone, recrystallised from chloroform–alcohol, separated in needles, m. p. 234—235°, turning yellow at 228° (Found: C, 77·3; H, 9·0; N, 7·9. $C_{35}H_{51}O_2N_3$ requires C, 77·1; H, 9·4; N, 7·7%).

*Dehalogenation of 5-Chlorocholestane-3 : 6-diol Dibenzoate*.—$\Delta^5$-Cholestene-3 : 6-diol dibenzoate (III, R = COPh) was prepared (a) according to Lettré and Müller (*loc. cit.*) by heating 5-chloro-3 : 6-dibenzoyloxycholestane (II; R = COPh, $R_1$ = Cl) (2 g.) for 2 hours at 210°/0·5 mm. Benzoic acid (0·24 g.) sublimed. The yellowish resinous residue crystallised on treatment with cold ether (10 c.c.), yielding a white solid (1·15 g.), m. p. 178—179°. On recrystallisation from ethyl acetate–methyl alcohol (1 : 1), prismatic needles of the enol-benzoate, m. p. 179—180°, were obtained.

(b) A solntion of 3-ketocholestanol (0·5 g.) and benzoic anhydride (1 g.) in benzoyl chloride (5 c.c.) was refluxed for 1½ hours. Benzoyl chloride was removed in a vacuum, and the residne dissolved in ether (5 c.c.). Crystallisation of the enol-benzoate began on addition of methyl alcohol (5 c.c.) and was complete at 0° after a few hours. The white product (0·4 g.) was recrystallised from ethyl acetate–methyl alcohol and was identical with the specimen prepared by method (a); m. p. 179—180°, $[\alpha]_D^{19°}$ + 6·9°, $[\alpha]_{5461}^{19°}$ + 8·7° (*c*, 1·342); $\alpha_{5461}/\alpha_D$ = 1·26 (Found : C, 80·3; H, 8·8. Calc. for $C_{41}H_{54}O_4$ : C, 80·6; H, 8·9%). The enol-benzoate gave a yellow colour with tetranitromethane and a violet Liebermann–Burchard reaction.

6-Ketocholestanol (VI) (= Lettré's " diol ") was obtained from the above enol-benzoate (a) (0·5 g.) by hydrolysis with alcoholic potassium hydroxide. In agreement with the statement of the German authors, the product melted at 137—138°. The m. p. was raised, however, to 142—143° after two recrystallisations from 95% methyl alcohol and was not depressed by authentic 6-ketocholestanol prepared by the original method of Mauthner or Windans (*loc. cit.*). The saturated keto-alcohol gave a violet Liebermann–Burchard reaction and was precipitated by digitonin (cf. Westphalen's diol above).

6-Keto-cholestanol (10 mg.) in alcohol (2 c.c.) containing 2 drops of acetic acid was heated with *o*-tolylsemicarbazide (8 mg.) on the steam-bath for ½ hour; the crystals (9·8 mg.) were collected after 24 hours, and recrystallised from spirit, *6-ketocholestanol-o-tolylsemicarbazone* separating in aggregates of fine needles, m. p. 223—224° (Found : C, 76·7; H, 9·9. $C_{35}H_{55}O_2N_3$ requires C, 76·7; H, 9·8%). The *p*-nitrophenylhydrazone, prepared by the usual technique, crystallised from methyl alcohol in yellow needles, m. p. and mixed m. p. 196—197°.

*3-Ketocholestanyl Benzoate from the Enol-benzoate*.—The enol-benzoate (0·3 g.), prepared by method (a), was hydrolysed as above, and the product (0·2 g.) benzoylated in pyridine solution with benzoyl chloride. After a few hours the well-formed crystals deposited were removed, washed with spirit, and recrystallised from acetone, yielding 3-ketocholestanyl benzoate (0·18 g.) in large transparent prisms, m. p. 179—180°, not depressed by a specimen prepared by the same method from 3-ketocholestanol (Windaus, *loc. cit.*, gives m. p. 173° for a specimen prepared by the Schotten–Baumann method) (Found : C, 80·4; H, 9·7. Calc. for $C_{34}H_{50}O_3$ : C, 80·6; H, 9·9%). A mixture of the benzoate with the enol-benzoate (a) of the same m. p. began to melt at 150° and was fused at 155°.

*3-Ketocholestanyl Acetate from the Enol-benzoate* (a).—The product (0·4 g.) obtained on hydrolysis of the enol-benzoate was refluxed with acetic anhydride (4 c.c.) for ½ hour; the acetate produced crystallised in elongated prisms, m. p. 129—130°, not depressed by an authentic specimen (Found : C, 78·2; H, 10·7. Calc. for $C_{29}H_{48}O_3$ : C, 78·3; H, 10·8%). The *p*-nitrophenylhydrazone separated in fine needles when a mixture of alcoholic solutions of the constituents was kept for 24 hours; it crystallised from methyl alcohol in yellow needles, m. p. 146—147°, unaltered on admixture with an authentic specimen (Found : C, 72·2; H, 9·0; N, 7·2. Calc. for $C_{35}H_{53}O_4N_3$ : C, 72·5; H, 9·2; N, 7·3%).

*Liebermann–Burchard Reaction of Saturated Steroid Ketones*.—The following gave a violet colour, showing a band at 5500—6000 A. : cholestan-6-one, α-chlorocholestan-6-one, β-chloro-cholestan-6-one, cholestanol-6-one (and its esters). Cholestane-3 : 6-dione gave a green colour but cholestan-3-one and coprostan-3-one remained colourless.

One of us (V. A. P.) is indebted to the Dixon Fund of London University for a grant.

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QUEEN MARY COLLEGE, LONDON. E. 1.
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## 121. *Long-chain Alkylpyridines and their Derivatives. New Examples of Liquid Crystals.*

By G. A. Knight and B. D. Shaw.

The methods which serve for the production of simple homologues of pyridine are inapplicable to long-chain compounds; the latter can be prepared by Tschitschibabin's method (condensation of 2-picoline with an alkyl chloride in presence of sodamide), provided that the reaction is carried out at 100°.

The products are wax-like solids, soluble in strong acids, to form salts which lather freely in aqueous solution. The hydrochlorides melt to form birefringent, anisotropic, viscous masses, which, at higher temperatures, pass abruptly into isotropic, mobile liquids. The corresponding 1-alkylpyridinium salts behave similarly.

The following are described: 1-n-*dodecylpyridinium chloride, bromide* and *iodide*; 1-n-*tetradecylpyridinium chloride* and *iodide*; 1-cetylpyridinium chloride and iodide; 1-n-*octadecylpyridinium chloride* and *iodide*; 2-n-*tridecyl-*, 2-n-*pentadecyl-*, 2-n-*heptadecyl-*, and 2-n-*nonadecyl-pyridine*, and the *hydrochlorides, picrates*, and *picrolonates* of these bases.

Prior to the publication by Tschitschibabin (*Bull. Soc. chim.*, 1936, **3**, 1607) of the method which he justly claims must take first place among reactions for the preparation of 2- and 4-alkylpyridines, the authors had tried in vain to prepare long-chain 2-alkyl derivatives of pyridine which were required for another investigation. Dodecylpyridinium chloride decomposed at 200°, in the presence of copper, forming dodecylene and pyridinium chloride; attempted condensation of dodecyl alcohol with pyridine in presence of zinc chloride gave a similar result; and tridecaldehyde yielded no condensation product with 2-picoline.

Tschitschibabin obtained good yields of bases such as 2-*n*-amylpyridine by condensing simple chlorides with 2-picoline in presence of sodamide at room temperature; bromides and iodides gave much lower yields owing to quaternary salt formation. The authors have repeated some of Tschitschibabin's work with these simple halides and find that his claims are fully justified.

Extension of the method to long-chain halides, however, gave negligible yields in 72 hours, and the reaction was incomplete after 12 weeks. Yields of 47—70% of the theoretical were obtained by conducting the reaction at 100° during 24 hours; quaternary chloride formation at this temperature is negligible.

The long-chain 2-alkylpyridines are feeble bases whose salts with strong acids resemble soaps in lathering freely in aqueous solution, and acting as emulsifying agents. The hydrochlorides melt to form viscous liquids which, under the microscope, between crossed nicols, exhibit birefringence and anisotropic colours. At higher temperatures they pass abruptly into mobile isotropic liquids. This property is not shown by the free bases, or by their picrates or picrolonates.

Tschitschibabin obtained, as by-products, compounds formed by the condensation of two mols. of alkyl chloride with one of 2-picoline. No such compounds were obtained in the present investigation owing, no doubt, to the low reactivity of long-chain chlorides.

The long-chain 1-alkylpyridinium salts are readily soluble in water, the solutions foam readily, form more stable emulsions with oils than either soaps or sodium alkyl sulphates containing the same number of carbon atoms in the open chain, and impart a greasy appearance to the surface of glass. These salts also form liquid crystals.

### Experimental.

*Quaternary Salts.*—Alkyl chlorides were heated with pyridine for 8 hours at 150°, the bromides required 1 hour at 150°, and the iodides 3 hours at 100°. Dodecyl chloride, heated with pyridine at 100° for 24 hours, gave a product containing only 1·7% of the theoretical amount of ionisable chlorine. The iodides were also prepared by treating the chlorides with potassium iodide in concentrated aqueous solution. The salts were crystallised by solution in the minimum quantity

of dry alcohol, dilution with dry ether, and cooling (to 0° for the dodecyl compounds). The solubility in water and in alcohol diminishes with increase in length of the hydrocarbon chain, but that in benzene increases. The two m. p.'s are recorded as I and II. 1-*Dodecylpyridinium chloride*, m. p. I, 71°, II, 145° (Found : Cl, 12·2. $C_{17}H_{30}NCl$ requires Cl, 12·5%), *bromide*, m. p. I, 89—90°, II, 125° (Found : Br, 24·1. $C_{17}H_{30}NBr$ requires Br, 24·4%), *iodide*, m. p. I, 88—89°, II, 93° (Found : I, 33·6. $C_{17}H_{30}NI$ requires I, 33·9%). 1-*Tetradecylpyridinium chloride*, m. p. I, 77°, II, 205° (Found : Cl, 11·0. $C_{19}H_{34}NCl$ requires Cl, 11·4%), *iodide*, m. p. I, 94°, II, 155° (Found : I, 31·2. $C_{19}H_{34}NI$ requires I, 31·5%). 1-Cetylpyridinium chloride, m. p. I, 83°, II, 217° (Found : Cl, 10·3. $C_{21}H_{38}NCl$ requires Cl, 10·5%), iodide, m. p. I, 98°, II, 205° (Found : I, 29·4. $C_{21}H_{38}NI$ requires I, 29·5%); Macovski (*Bull. Soc. chim.*, 1936, **3**, 498) gives m. p. 110° for the chloride, and 101° for the iodide. 1-*Octadecylpyridinium chloride*, m. p. I, 89°, II, 220° (Found : Cl, 9·4. $C_{23}H_{42}NCl$ requires Cl, 9·7%), *iodide*, m. p. I, 103°, II, 221° (Found : I, 27·5. $C_{23}H_{42}NI$ requires I, 27·7%).

2-n-*Tridecylpyridine*.—2-Picoline (23·0 g.; 1·0 mol.) and finely divided sodamide (10 g.; 1·0 mol.) were stirred mechanically in a flask with a mercury seal; the mixture became yellow, then deep red. *n*-Dodecyl chloride (34·0 g.; 0·6 mol.) was added slowly, and the mixture maintained at 100° for 24 hours, with frequent stirring. Isolation of the product presented difficulty at first. 2N-Hydrochloric acid extracted very little of the new base, and more concentrated acid produced a semi-solid, soap-like mass, which included unchanged dodecyl chloride. Precipitation as the perchlorate was fairly satisfactory, but yielded a slimy mass which was difficult to manipulate. The following method was adopted finally; the crude product, after decomposition of unchanged sodamide with water, and removal of 2-picoline in steam, was extracted with petroleum (b. p. 60—80°; 300 c.c.). The extract was dried over sodium sulphate, and the hydrochloride precipitated with dry hydrogen chloride, washed with petroleum, and decomposed with hot 10% sodium hydroxide solution. On distillation, 95% of the total yield had b. p. 335—336° and solidified to a wax-like solid (39 g.). Purified *via* the picrate, the *base* had m. p. 19°, b. p. 199°/10 mm. (Found : C, 82·6; H, 11·9; N, 5·4. $C_{18}H_{31}N$ requires C, 82·8; H, 11·9; N, 5·4%). The *hydrochloride* had m. p. I, 52°, II, 109° (Found : Cl, 11·8. $C_{18}H_{31}N,HCl$ requires Cl, 11·9%). The *picrate*, precipitated from alcohol–acetone and recrystallised from ethyl acetate, had m. p. 78° (Found : C, 58·8; H, 7·0. $C_{18}H_{31}N,C_6H_3O_7N_3$ requires C, 58·8; H, 6·9%), and the *picrolonate*, from alcohol, had m. p. 85° (Found : C, 63·9; H, 7·7. $C_{18}H_{31}N,C_{10}H_8O_5N_4$ requires C, 64·0; H, 7·4%). The other bases and their salts were prepared and purified by similar methods.

2-Picoline (45 g.), sodamide (20 g.), and *n*-tetradecyl chloride (78 g.) gave 2-n-*pentadecylpyridine* (43 g.), m. p. 29°, b. p. 215°/10 mm. (Found : C, 83·1; H, 12·0; N, 4·8. $C_{20}H_{35}N$ requires C, 83·1; H, 12·1; N, 4·8%); *hydrochloride*, m. p. I, 59°, II, 118° (Found : Cl, 10·7. $C_{20}H_{35}N,HCl$ requires Cl, 10·9%); *picrate*, m. p. 85° (Found : C, 60·7; H, 7·5. $C_{20}H_{35}N,C_6H_3O_7N_3$ requires C, 60·2; H, 7·3%); *picrolonate*, m. p. 92° (Found : C, 64·9; H, 7·6. $C_{20}H_{35}N,C_{10}H_8O_5N_4$ requires C, 65·1; H, 7·8%).

2-Picoline (46 g.), sodamide (20 g.), and *n*-hexadecyl chloride (75 g.) gave 2-n-*heptadecylpyridine* (48 g.), m. p. 37°, b. p. 231°/10 mm. (Found : C, 83·1; H, 12·3; N, 4·5. $C_{22}H_{39}N$ requires C, 83·3; H, 12·3; N, 4·4%); *hydrochloride*, m. p. I, 65°, II, 125° (Found : Cl, 9·9. $C_{22}H_{39}N,HCl$ requires Cl, 10·0%); *picrate*, m. p. 85—86° (Found : C, 61·7; H, 7·9. $C_{22}H_{39}N,C_6H_3O_7N_3$ requires C, 61·5; H, 7·7%); *picrolonate*, m. p. 95·5° (Found : C, 66·0; H, 8·2. $C_{22}H_{39}N,C_{10}H_8O_5N_4$ requires C, 66·1; H, 8·1%).

2-Picoline (46 g.), sodamide (20 g.), and *n*-octadecyl chloride (96 g.) gave 2-n-*nonadecylpyridine* (40 g.), m. p. 46°, b. p. 247—248°/10 mm. (Found : C, 83·2; H, 12·3; N, 4·3. $C_{24}H_{43}N$ requires C, 83·5; H, 12·5; N, 4·1%); *hydrochloride*, m. p. I, 73°, II, 134° (Found : Cl, 9·2. $C_{24}H_{43}N,HCl$ requires Cl, 9·3%); *picrate*, m. p. 93—94° (Found : C, 62·8; H, 7·7. $C_{24}H_{43}N,C_6H_3O_7N_3$ requires C, 62·7; H, 8·0%); *picrolonate*, m. p. 99—100° (Found : C, 67·0; H, 8·4. $C_{24}H_{43}N,C_{10}H_8O_5N_4$ requires C, 67·0; H, 8·4%).

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UNIVERSITY COLLEGE, NOTTINGHAM. [*Received, March 15th, 1938.*]

# 122. *The Condensation of* p-*Toluenesulphinic Acid and its Esters with Acetone.*

By C. L. ARCUS and J. KENYON.

*p*-Toluenesulphinic acid and its esters condense with acetone to produce p-*tolyl*-β-(β-*methylpentan*-δ-*onyl*)*sulphone* (I) and evidence supporting this formulation of the condensation product is given. Further evidence is adduced that the condensation proceeds, not by an exchange of carbonium kations, but probably by a rearrangement of diacetonyl *p*-toluenesulphinate which results from alcoholysis of the sulphinic esters by the diacetonyl alcohol present in the equilibrium mixture.

DURING an investigation of the molecular rearrangement of phenylmethylcarbinyl *p*-toluenesulphinate (Arcus, Balfe, and Kenyon, this vol., p. 485) the condensation of this ester, and also of β-octyl *p*-toluenesulphinate, with acetone was observed; it was known from a previous unpublished investigation in this laboratory that ethyl *p*-toluenesulphinate and *p*-toluenesulphinic acid condense with acetone. These observations have been correlated and are now presented.

From a solution of *p*-toluenesulphinic acid in acetone there separates, after heating, a compound, m. p. 94°, which has been identified as p-*tolyl*-β-(β-*methylpentan*-δ-*onyl*)*sulphone* (I) on the following evidence. It contains no free hydroxyl group, since it does not undergo acetylation, but contains a carbonyl group, since it furnishes a *semicarbazone*, from which the original ketone is regenerated by hydrolysis. It is a sulphone and not a sulphinic ester, since it is not oxidised by perhydrol, a reagent which converts sulphinates into sulphonates. It may be oxidised with acid permanganate solution, but the only product isolable is *p*-sulphobenzoic acid.

Decomposition with aqueous alkali yields *p*-toluenesulphinic acid and mesityl oxide, the latter indicating the nature of the aliphatic portion of the molecule.

Finally this compound may be synthesised by the slow condensation of *p*-toluenesulphinyl chloride with diacetone alcohol:

$$CMe_2(OH)\cdot CH_2\cdot CO\cdot CH_3 + C_7H_7\cdot SOCl \longrightarrow CMe_2(SO_2\cdot C_7H_7)\cdot CH_2\cdot CO\cdot CH_3 \quad \text{(I.)}$$

The sulphinic esters do not condense with acetone nearly so readily as the free acid, since di-*p*-tolyl disulphoxide is the only isolable product after ethyl *p*-toluenesulphinate has been heated in acetone solution. On prolonged keeping at room temperature of solutions in acetone of ethyl, β-octyl, and phenylmethylcarbinyl *p*-toluenesulphinates, however, condensation to *p*-tolyl-β-(β-methylpentan-δ-onyl)sulphone occurs. The alcohols displaced in the last two cases have been isolated.

In view of the last result, and also of the non-formation either of olefinic compounds or of ethyl-, β-octyl-, and α-phenylethyl-sulphones, dissociation of the sulphinic esters to give carbonium kations is improbable, *e.g.*,

$$C_7H_7\cdot S{\nearrow O \atop \searrow OR} \rightleftharpoons C_7H_7\cdot \overset{-}{SO_2} + \overset{+}{R} \longrightarrow C_7H_7\cdot \overset{O\uparrow}{\underset{O\downarrow}{S}}R$$

also

$$\overset{+}{R} \longrightarrow \overset{+}{H} + \text{olefin}$$

In the presence of a constant equilibrium proportion of diacetone alcohol, alcoholysis of the sulphinic esters will occur, without rupture of the O–R bond; such alcoholyses have been observed for (—) phenylmethylcarbinyl *p*-toluenesulphinate (Kenyon and Phillips, J., **1930**, **1676**) and for ethyl *p*-toluenesulphinate by *l*-β-octyl alcohol (Phillips, J., **1925**, **127**, 2552). The *p*-toluenesulphinic ester of diacetone alcohol first produced can then undergo rearrangement into *p*-tolyl-β-(β-methylpentan-δ-onyl)sulphone, as it appears to do during the synthesis of this substance from diacetone alcohol and *p*-toluenesulphinyl chloride.

## Experimental.

*The Interaction of Ethyl* p-*Toluenesulphinate and Acetone.*—(a) *At the ordinary temperature.* A solution of ethyl *p*-toluenesulphinate (17 g.) in acetone (75 c.c.) was kept in a closed vessel for 5 years. On evaporation of the solution, crystalline leaflets (23·3 g.), m. p. 72—75°, separated, which after recrystallisation from ether had m. p. 94° (Found: C, 61·6; H, 7·3; S, 13·3. $C_{13}H_{18}O_3S$ requires C, 61·4; H, 7·1; S, 12·6%).

(b) *At higher temperatures.* A solution of ethyl *p*-toluenesulphinate (3 g.) in acetone (15 c.c.) was heated under reflux for an hour and then kept at the ordinary temperature for several days. The crystals (0·8 g.) which separated consisted entirely of di-*p*-tolyl disulphoxide, m. p. 76°.

*The Interaction of* dl-*Phenylmethylcarbinyl* p-*Toluenesulphinate and Acetone.*—A solution of *dl*-phenylmethylcarbinyl *p*-toluenesulphinate (7·5 g.) in acetone (25 g.) was kept at the ordinary temperature for 7 months. On evaporation, crystals separated, which had m. p. 87—90° (2·6 g.) after washing with light petroleum, m. p. 94° after recrystallisation from benzene (Found: S, 12·2%), and furnished the semicarbazone, m. p. 173° (decomp.), by the method described below. The light-petroleum wash-liquor yielded phenylmethylcarbinol (1 g.), b. p. 70°/20 mm., $n_D^{20°}$ 1·5243.

*The Interaction of* dl-β-*Octyl* p-*Toluenesulphinate and Acetone.*—A solution of *dl*-β-octyl *p*-toluenesulphinate (5 g.) in acetone (30 c.c.) was kept for 6 months. The crystalline residue obtained on evaporation was washed with ethyl alcohol and recrystallised, yielding colourless plates (2·0 g.), m. p. 94° alone and when mixed with the product of the condensation of *dl*-phenylmethylcarbinyl *p*-toluenesulphinate with acetone. The substance furnished the semicarbazone, m. p. 172° (decomp.). From the alcoholic wash-liquor, *dl*-β-octyl alcohol (1 g.), b. p. 81°/20 mm., $n_D^{20°}$ 1·4285, was obtained.

*The Interaction of* p-*Toluenesulphinic Acid and Acetone.*—A solution of *p*-toluenesulphinic acid (7 g.) in dry acetone (30 c.c.) was gently heated for 1 hour and then allowed to evaporate at the ordinary temperature; crystals separated which, after washing with sodium carbonate solution and recrystallisation from ether, had m. p. 94° (4·8 g.).

p-*Tolyl*-β-(β-*methylpentan*-δ-*onyl*)*sulphone.*—The compound, m. p. 94°, which separated during the above reactions is assigned the structure of p-*tolyl*-β-(β-*methylpentan*-δ-*onyl*)*sulphone* and undergoes the following reactions.

It is slightly soluble in boiling water, from which, on cooling, it crystallises in leaflets. It separates unchanged from a warm solution in acetic anhydride, and is unaffected by perhydrol in acetone solution. It is oxidised by potassium permanganate in warm acetic acid solution, but the only product which could be isolated was *p*-sulphobenzoic acid, m. p. 257—259° (decomp.).

The compound (3 g.) was added to sodium carbonate (1 g.) in aqueous solution and the distillate obtained on passing a current of steam was warmed with semicarbazide hydrochloride (2 g.) and sodium carbonate (1 g.); on cooling, crystals (0·75 g.), m. p. 156°, of mesityl oxide semicarbazone separated. From the residual liquor of the steam distillation, on acidification, *p*-toluenesulphinic acid (1·7 g.), m. p. 86°, was obtained.

The compound (5 g.), when heated in aqueous alcoholic solution with semicarbazide hydrochloride (5 g.) and sodium acetate (4·2 g.), furnished leaflets (5·0 g.), which on recrystallisation from hot alcohol yielded the *semicarbazone* of *p*-tolyl-β-(β-methylpentan-δ-onyl)sulphone, m. p. 173° (decomp.) (Found: C, 53·4; H, 6·8; S, 9·9. $C_{14}H_{21}O_3N_3S$ requires C, 54·0; H, 6·8; S, 10·3%).

This semicarbazone is unaffected by hot aqueous alcoholic solutions of either oxalic acid or sodium hydroxide, but is rapidly hydrolysed on dissolution in cold concentrated hydrochloric acid, from which crystals, m. p. 94° alone or mixed with the original compound, separate after a few seconds.

*Preparation of* p-*Tolyl*-β-(β-*methylpentan*-δ-*onyl*)*sulphone from Diacetone Alcohol and* p-*Toluenesulphinyl Chloride.*—*p*-Toluenesulphinyl chloride (9·0 g.) was added in portions to an ice-cold mixture of diacetone alcohol (5·8 g.) and pyridine (4·5 g.), and the whole kept at the ordinary temperature for 5 weeks. The solid product was then triturated with dilute hydrochloric acid and recrystallised from ether, forming leaflets (5·0 g.), m. p. 94° alone or when mixed with the compound obtained by the interaction of acetone and ethyl *p*-toluenesulphinate.

Thanks are expressed to the Government Grants Committee of the Royal Society and to Imperial Chemical Industries, Ltd., for grants. One of the authors (C. L. A.) is indebted to the Department of Scientific and Industrial Research for a maintenance grant.

Battersea Polytechnic, London, S.W. 11. [Received, March 21st, 1938.]

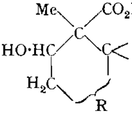
## 123. *The Triterpene Group. Part I. β-Boswellic Acid.*

By James C. E. Simpson and Norman E. Williams.

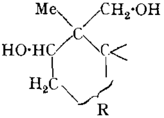
Derivatives of the triterpene acid β-boswellic acid are described which demonstrate that it is a β-hydroxy-acid, in contrast to the statement of Trost (*Ann. Chim. Appl.*, 1937, **27**, 178) that it is an α-hydroxy-acid.

β-Boswellic acid, one of the principal triterpenoid constituents of frankincense, was first isolated in the pure state by Winterstein and Stein (*Z. physiol. Chem.*, 1932, **208**, 9) and characterised by them as a monobasic monohydroxy-acid, $C_{30}H_{48}O_3$. Although no work on the detailed structure of this acid has yet been published, the results obtained by Beaucourt (*Monatsh.*, 1930, **55**, 185) from selenium dehydrogenation of the (impure) acid indicate that it belongs to the important group represented by hederagenin, oleanolic acid, gypsogenin, the amyrins, and sia- and suma-resinolic acids; in particular, the hydrocarbon, m. p. 305°, isolated by Beaucourt (*loc. cit.*) is probably identical (see Ruzicka *et al.*, *Helv. Chim. Acta*, 1932, **15**, 431) with 1 : 8-dimethylpicene (Ruzicka and Hofmann, *ibid.*, 1937, **20**, 1155).

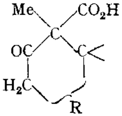
It was recently found in this laboratory that β-boswellic acid is converted by fairly mild oxidation with chromic anhydride into a ketone, $C_{29}H_{46}O$, for which the name *nor-β-boswellenone* is suggested. On the other hand, methyl β-boswellate, $C_{31}H_{50}O_3$, is oxidised under similar conditions to the corresponding *keto-ester*, $C_{31}H_{48}O_3$. These results indicate, as pointed out by one of us (Simpson, *Nature*, 1937, **140**, 467), that β-boswellic acid is a β-hydroxy-acid (I, $R = C_{24}H_{40}$), which on oxidation passes into nor-β-boswellenone (IV, $R = C_{24}H_{40}$) *via* the intermediate keto-acid (III, $R = C_{24}H_{40}$). The ketonic nature of the oxygen atom in nor-β-boswellenone has been diagnosed by the formation of an *oxime* and also by the facile conversion of the ketone into the corresponding hydrocarbon, *nor-β-boswellene*, on Clemmensen reduction. The partial structure (I, $R = C_{24}H_{40}$) for β-boswellic acid is supported by the striking analogy between the oxidation already referred to and that of hederagenin methyl ester (II, $R = C_{25}H_{40}O_2$) previously studied by Jacobs and Gustus (*J. Biol. Chem.*, 1926, **69**, 641), which undergoes a parallel transformation to the corresponding ketone (IV, $R = C_{25}H_{40}O_2$) by way of the intermediate (III, $R = C_{25}H_{40}O_2$).



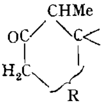

(I.)




(II.)




(III.)




(IV.)

Nor-β-boswellenone and the methyl ester of the acid (III, $R = C_{24}H_{40}$) have also been prepared by Trost (*Ann. Chim. Appl.*, 1937, **27**, 178) by oxidation of β-boswellic acid and its ester respectively. This author, however, states that the acid is an α-hydroxy-acid (V) and that nor-β-boswellenone is an aldehyde (VII) formed from (V) *via* the keto-acid (VI). Trost's conclusions must be regarded as unjustified for the following reasons: (i) The

$$C_{28}H_{45}\cdot CH(OH)\cdot CO_2H \qquad C_{28}H_{45}\cdot CO\cdot CO_2H \qquad C_{28}H_{45}\cdot CHO$$

(V.) (VI.) (VII.)

group $CH(OH)\cdot CO_2H$ does not account for the fact, observed both by Trost and by Winterstein and Stein (*loc. cit.*), that methyl β-boswellate is highly resistant to saponification; (ii) nor-β-boswellenone was not shown by Trost to possess aldehydic properties (we have in fact found that it has no such properties); (iii) the isolation of an aldehyde in quantity is improbable under the conditions obtaining in Trost's experiment (chromic anhydride–acetic acid at 90°); (iv) the significance of the analogous oxidation of hederagenin methyl ester is entirely disregarded.

Definite proof that Trost's hypothesis is indeed untenable has been furnished by the results of the further degradation of nor-β-boswellenone now in progress. The ketone is smoothly oxidised by permanganate in acetic acid to a new *ketone*, for which analytical data indicate the formula $C_{26}H_{42}O_2$. Acid products, which would be expected to predominate were nor-β-boswellenone an aldehyde, are formed only in traces. This ketone differs markedly in its colour reactions from its precursor and from β-boswellic acid; its structure will be discussed in a future communication.

## Experimental.

(Melting points uncorrected; specific rotations in chloroform.)

β-Boswellic acid was prepared by the method of Winterstein and Stein (*loc. cit.*), a 2% yield of the pure acid, m. p. 233—234°, being obtained.

*Methyl β-Boswellate.*—Esterification of the acid with ethereal diazomethane yielded the ester as prisms (from chloroform–methanol), m. p. 195—195·5°, $[\alpha]_D^{14°}$ +161°, +160° ($l$ = 1, $c$ = 0·96, 2·55). Winterstein and Stein give m. p. 189—190° (corr.), $[\alpha]_D^{19°}$ +116°; Trost records m. p. 198—200° (corr.), $[\alpha]_D^{20°}$ +145° [Found (all analyses by Weiler): C, 78·85; H, 10·5; OMe, 6·3. Calc. for $C_{31}H_{50}O_3$: C, 79·1; H, 10·7; OMe, 6·6%].

*Oxidation of Methyl β-Boswellate.*—A solution of the ester (0·5 g.) in glacial acetic acid (100 c.c.) and water (10 c.c.) was stirred at 50° while chromic anhydride (0·2 g. in 2 c.c. of water and 10 c.c. of acetic acid) was run in during 20 minutes; the temperature was slowly raised and maintained at 70° for a further hour. Methyl alcohol was then added, the solvent removed under reduced pressure, and the residue, after addition of very dilute sulphuric acid and extraction with ether, separated into acid and neutral fractions with 3% sodium hydroxide solution. The latter fraction separated from methyl alcohol in long, brittle, needle-like rods of the *keto-ester*, m. p. 159—160° after several crystallisations [Trost gives m. p. 155—157° (corr.)] (Found: C, 79·1; H, 10·2. $C_{31}H_{48}O_3$ requires C, 79·4; H, 10·3%).

The *oxime* crystallised from aqueous alcohol in soft slender needles; it melted at 202° to a turbid liquid which cleared at 210° [Trost, m. p. 194—196° (corr.)] (Found: N, 3·3. $C_{31}H_{49}O_3N$ requires N, 2·9%).

*Nor-β-boswellenone.*—A solution of β-boswellic acid (10 g.) in glacial acetic acid (500 c.c.) and water (50 c.c.) was stirred mechanically while a solution of chromic anhydride (4 g. in 150 c.c. of acetic acid and 30 c.c. of water) was added during 1 hour at 55°. After a further 1½ hours at this temperature the product was worked up as in the oxidation of methyl β-boswellate; the ketone separated in needles from an alcoholic solution of the neutral fraction, and had m. p. 195—196° [Trost gives 200—202° (corr.)] after recrystallisation (yield, 35%). In our hands the conditions employed by Trost for the preparation of this compound gave a much inferior yield of pure material, although Trost states that the (presumably crude) product was isolated in 90% yield (Found: C, 84·8; H, 11·1. $C_{29}H_{46}O$ requires C, 84·8; H, 11·3%). *Nor-β-boswellenone* gives a yellow coloration with tetranitromethane in chloroform, and a wine-red colour with the Liebermann–Burchard reagent. Negative reactions were obtained with the Schiff and the Tollens reagent. $[\alpha]_D^{12°}$ +128° ($l$ = 1, $c$ = 1·065).

The *oxime* crystallised from methanol in clusters of minute needles, m. p. 164—167° [Trost, m. p. 196—197° (corr.)] (Found: C, 81·3; H, 10·7; N, 3·4. $C_{29}H_{47}ON$ requires C, 81·8; H, 11·1; N, 3·3%).

*Nor-β-boswellene.*—Nor-β-boswellenone (0·1 g.) in glacial acetic acid (12 c.c.) was refluxed for 3 hours with amalgamated zinc (1·2 g.) and concentrated hydrochloric acid (6 c.c.). The *hydrocarbon* was obtained by dilution of the filtered solution and was recrystallised from chloroform–methanol and finally from acetone; it formed clusters of needles, m. p. 168—169° (yield, 80%) (Found: C, 87·7; H, 12·4. $C_{29}H_{48}$ requires C, 87·8; H, 12·2%). It gave a yellow colour with tetranitromethane in chloroform, and a crimson-mauve Liebermann–Burchard reaction. $[\alpha]_D^{12°}$ +143° ($l$ = 1, $c$ = 0·99).

*Further Oxidation of Nor-β-boswellenone.*—The ketone (2 g.) was dissolved in glacial acetic acid (200 c.c.) and treated with 50 c.c. of N-potassium permanganate (≡ *ca.* 5 O), added drop by drop with stirring during 1 hour at 48°. After a further ½ hour the solution was clarified with sodium bisulphite, diluted with water, and extracted with ether. The extract was shaken with 3% sodium hydroxide solution, washed, dried, and evaporated. A methyl-alcoholic solution of the residue (1·8 g.) deposited the new *ketone* in colourless needles, m. p. 217—218° after recrystallisation (yield, 45%); $[\alpha]_D^{11°}$ +157° ($l$ = 1, $c$ = 0·90) (Found: C, 80·7, 81·0; H, 10·5, 10·6. $C_{26}H_{42}O_2$ requires C, 80·8; H, 11·0%). The substance gave no coloration with tetranitromethane

in chloroform, and only a yellowish-brown colour with the Liebermann–Burchard reagent. It was recovered unchanged, although in rather small yield, after refluxing for 2 hours with 1% alcoholic potash.

On treatment with hydroxylamine acetate under the usual conditions a *product* was formed which crystallised from aqueous methanol in small needles, m. p. 197—198° (Found: C, 78·85, 79·4; H, 10·3, 10·5; N, 4·0, 3·6, 4·0%).

The *semicarbazone*, prepared by refluxing for 3 hours a solution of the ketone in methyl alcohol with semicarbazide acetate, was crystallised from aqueous methanol and finally from benzene–ligroin, from which it separated in clusters of needles, m. p. 238—239° (Found: C, 73·5; H, 9·95; N, 8·7. $C_{27}H_{45}O_2N_3$ requires C, 73·1; H, 10·2; N, 9·5%).

University of London, King's College. [*Received, March 21st*, 1938.]

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# 124. *Studies in Chemisorption on Charcoal. Part X. Hydrolytic Adsorption.*

By H. H. Chambers and A. King.

The influence of temperature of activation on the hydrolytic and molecular adsorption of salts by pure sugar charcoal has been studied. Curves are given showing how adsorption per unit area varies with temperature of activation. These curves are continuous, and they show that the fundamental difference between high- and low-temperature charcoals is that the former liberate bases from salts whereas the latter liberate acids. Various factors affecting the shape of the curves are discussed, and it is pointed out that the surface oxide theory cannot give a detailed account of the mechanism of hydrolytic adsorption although it does account for the general trend of the results. The results for different salts are in agreement with observations of previous workers that salts of strong acids and weak bases or strong bases and weak acids are adsorbed both hydrolytically and molecularly, but salts of strong acids and strong bases are adsorbed only hydrolytically.

It has been known for a considerable time that salts are sometimes hydrolytically adsorbed from aqueous solution by activated charcoal. If, for example, a charcoal activated at a high temperature is placed in a solution of a neutral salt, some of the acid formed by the hydrolysis of the salt is preferentially adsorbed and an equivalent amount of free alkali is left in solution. Thus even a salt formed from a strong acid and strong base may be completely hydrolysed by removal of one of the hydrolysis products by adsorption. Much of the early work on the subject was carried out on impure charcoals, and the results are, on the whole, inconclusive and often contradictory. The first really conclusive work was that of Bartell and Miller (*J. Amer. Chem. Soc.*, 1922, **44**, 1866; 1923, **45**, 1106), who measured the hydrolytic adsorption of methylene-blue and of salts of various acid dyes by pure sugar charcoal activated at 1000°. In 1924 Miller (*ibid.*, **46**, 1150) was able to show that after adsorption from sodium benzoate solution, the amount of acid in the charcoal was exactly equivalent to the amount of free alkali in the solution (with a 1200° charcoal). Kolthoff (*Rec. Trav. chim.*, 1927, **46**, 549; *Z. Elektrochem.*, 1927, **33**, 497), as a result of work on charcoals activated between 900° and 1000°, formulated a set of rules for hydrolytic adsorption of salts with reference to the capillary activity of the acids and bases from which the salts are formed. Various other workers have investigated the problem from different viewpoints, but almost without exception, the work has been carried out unsystematically and only on high-temperature charcoals.

Previous work in the present series has shown that the properties of charcoal vary very greatly with temperature of activation, the fundamental difference between high- and low-temperature charcoals being brought out very clearly by the results for the adsorption of acids and bases (Part IX, J., 1937, 1489). It was found that a 900° charcoal possessed maximum acid- and minimum base-adsorbing properties, the reverse being true of a 400° charcoal. At intermediate temperatures there was a gradual change from one type of charcoal to the other. These results suggested the subject of the present research. It

seemed improbable that hydrolytic adsorption should be exclusively a property of high-temperature charcoals, and likely that low-temperature charcoals would exhibit hydrolytic adsorption in the opposite direction to that of high-temperature charcoals, while at some intermediate temperature the hydrolytic adsorption would be zero. This has proved to be the case.

In view of the fact that, in general, organic acids and bases are very much more strongly adsorbed than inorganic acids and bases, it was decided to study the following three typical cases: (1) a salt of an inorganic base and an organic acid (sodium benzoate); (2) a salt of an organic base and an inorganic acid (methylene-blue); and (3) a salt of an inorganic acid and an inorganic base (potassium chloride). Both hydrolytic adsorption and molecular adsorption were measured with ten charcoals activated at temperatures ranging from 320° to 1100°. The results are given in the table. Results for molecular adsorption are expressed in all cases as amount of substance in equiv. $\times 10^{-5}$ adsorbed per g. of charcoal, and for hydrolytic adsorption as amount of acid or base in equiv. $\times 10^{-5}$ liberated per g. of charcoal. A negative sign indicates acid liberation, and a positive sign base liberation. The last two sets of results are for charcoals activated at the first of the two temperatures named and

| Temp. of activation. | Adsorption of KCl. | | Adsorption of sodium benzoate. | | Adsorption of methylene-blue. | | Adsorption of iodine. |
|---|---|---|---|---|---|---|---|
| | Hydrolytic. | Molecular. | Hydrolytic. | Molecular. | Hydrolytic. | Molecular. | |
| 320° | − 1·21 | (+ 1·7) | 0 | 22·5 | − 0·55 | 2·38 | 215 |
| 410 | − 1·60 | ( 0 ) | 0 | 16·0 | − 0·62 | 5·70 | 241 |
| 440 | − 1·98 | ( 0 ) | 0 | 14·9 | − 0·65 | 16·0 | 348 |
| 500 | + 0·12 | (+ 0·1) | 0 | 9·5 | 0 | 8·65 | 308 |
| 590 | + 0·83 | (+ 0·5) | + 0·82 | 3·5 | + 0·8 | 9·90 | 388 |
| 740 | + 1·64 | (+ 0·4) | + 2·88 | 10·0 | + 1·9 | 10·1 | 309 |
| 810 | + 3·45 | (− 0·3) | + 11·6 | 43·0 | + 1·1 | 117 | 974 |
| 880 | + 2·35 | (+ 1·0) | + 11·5 | 43·3 | + 1·1 | 76 | 911 |
| 980 | + 1·66 | ( 0 ) | + 4·12 | 42·7 | + 0·4 | 125 | 627 |
| 1100 | + 1·51 | (− 0·1) | + 6·57 | 34·0 | + 0·2 | 85 | 586 |
| 880, 410 | − 4·94 | ( 0 ) | 0 | 42·7 | − 26 | 121 | 726 |
| 410, 880 | + 3·43 | (+ 0·2) | + 11·6 | 45·2 | + 1·1 | 160 | 928 |

reactivated at the second. The adsorption of iodine from N/50-solution was also measured in order to obtain an estimate of the surface areas of each charcoal. By dividing all the values of hydrolytic and molecular adsorption by the corresponding iodine values, values were obtained which were taken as a measure of the adsorption per unit area. These values are plotted against temperature of activation in Figs. 1, 2, and 3. The results are

Fig. 1.

*Adsorption of potassium chloride.*

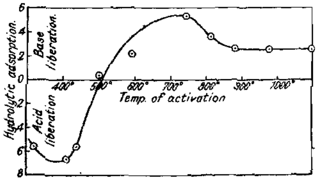
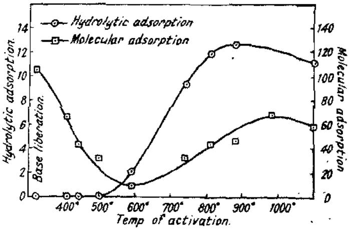



Fig. 2.

*Adsorption of sodium benzoate.*



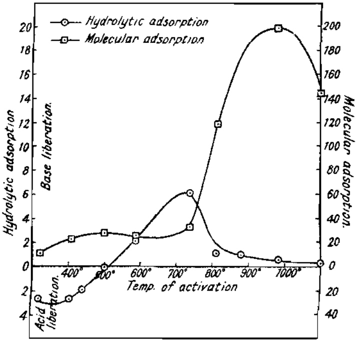

to a large extent independent of the extent of the surface (except possibly in cases where steric affects are present, as mentioned below) and depend only upon the nature of the charcoal surface. Consequently, they allow a comparison to be made between samples of charcoal activated at different temperatures.

The graphs show very clearly the difference between high- and low-temperature char-

coals. Potassium choride and methylene-blue both show definite hydrolytic adsorption with maxima for charcoals activated at 350—400° (acid liberation), and 700—750° (base liberation). At present no explanation can be given of the fact that the second maximum for these two salts does not correspond with charcoals possessing maximum acid-adsorbing properties, *i.e.*, with charcoals activated at 850—900°. Presumably this shift of the maximum is connected in some way with the chloride ion, because in both cases the acid which is being adsorbed is hydrochloric acid (methylene-blue is the hydrochloride of a basic dye). Sodium benzoate gives a maximum at about 800°, and no hydrolytic adsorption below 500°. Below 500° very small amounts of acid were detected by titration, but the calculated results for adsorptiou per unit area were quite erratic. Although the amounts of charcoal used in the three cases varied considerably, the actual volumes of base used in the titrations were remarkably constant. The only other constant factor in the titrations was the volume of solution used, and it was suspected that the acid present was merely dissolved carbon dioxide, no attempt having been made to exclude this from the system. Calculation from the known solubility of carbon dioxide in water (at its partial pressure in the atmosphere) showed that this would account for the acidity actually measured. It was assumed, therefore, that no hydrolytic adsorption took place on charcoals activated below 500°. This is explained by the fact that comparatively large amounts of benzoic acid are adsorbed even by low-temperature charcoals (King, *loc. cit.*). Presumably both benzoic acid and sodium hydroxide are adsorbed at the same time, but the method of analysis used does not allow a distinction to be made between this type of adsorption and true molecular adsorption.

Fig. 3.

*Adsorption of methylene-blue.*




Sodium benzoate shows abnormally high values of molecular adsorption on low-temperature charcoals. Two factors contribute to this. In the first place, since the charcoal was prepared by heating sucrose to a comparatively high temperature, it will have acquired some of the properties of a high-temperature charcoal. At temperatures below about 400° the surface conditions characteristic of these temperatures are established quite slowly, and so the charcoal may retain some of the properties of high-temperature charcoals. If this happens, the amount of substance adsorbed may be greater than would be the case if the high-temperature surface had been completely destroyed. The second factor tending to increase the apparent molecular adsorption is the fact (see above) that below 500° benzoic acid and sodium hydroxide are adsorbed together.

The graph for methylene-blue shows a sudden sharp rise of molecular adsorption beyond 740° which may be attributed to steric effects (King, J., 1934, 1975). Above this point the ultra-pores, which are initially too small to admit the methylene-blue molecules, are sufficiently enlarged by oxidation to allow adsorption to take place. As would be expected from the size of the molecule, steric effects play a large part in the adsorption of methylene-blue. These effects are most striking in the case of hydrolytic adsorption below 500° where the large methylene-blue hydroxide molecules are being adsorbed. Activation at 880° followed by reactivation at 410° gave a 15-fold increase of hydrolytic adsorption. Molecular adsorption showed a 10-fold increase. This increase is due to the increase of available surface area by the enlarging of the ultra-pores at high temperature.

The results for the hydrolytic adsorption of methylene-blue by high-temperature

charcoals do not agree with those of Bartell and Miller (*loc. cit.*), who found that charcoal activated at 1000° liberated acid from methylene-blue solutions. It should be pointed out, however, that the results are not strictly comparable because the experimental conditions were quite different. Bartell and Miller used 0·0025M-solutions with sufficient charcoal nearly to decolorise the solution, whereas in the present work 0·02N-solutions were used and the amount of charcoal was sufficient to remove only a small part of the dye from the solution.

In agreement with Miller and Kolthoff, it was found that potassium chloride is only hydrolytically adsorbed. Owing to difficulties of estimating potassium chloride in dilute solutions, the results for molecular adsorption (given in parentheses in the table) show sometimes a small positive and sometimes a small negative value. The assumption that molecular adsorption is zero is justified by the magnitude of the results and the inconsistency of the sign.

The graphs for molecular adsorption of the other two salts are interesting because they indicate that, even in cases where adsorption is not directly affected by the existence of specific surface oxides, temperature of activation may still have a considerable influence on the amount of adsorption. Very little work has been done on this influence, and it is not possible to say whether the type of curve obtained in the present work is of fundamental significance, or whether it is the result of a large number of factors, such as those mentioned above, all operating at the same time.

The general trend of the results for hydrolytic adsorption may be interpreted by the surface oxide theory, although it is evident that the surface of active charcoal and the mechanism of adsorption are far more complex than the theory suggests. The results for the two reactivations demonstrate the reversibility of surface conditions. In cases where steric effects are absent, the results for reactivated samples are very close to those for samples activated in the ordinary way at one temperature. In such cases the properties of the charcoal are characteristic of its activation temperature and independent of previous heat treatment. (These remarks refer, of course, to adsorption per unit area.) That hydrolytic adsorption is due to the presence of chemisorbed oxygen on the charcoal is shown by the fact that a sample of unactivated charcoal gave no appreciable hydrolytic adsorption. Kolthoff also noted this fact. Again, Burstein and Frumkin (*Z. physikal. Chem.*, 1929, **141**, 219) found that a sample of activated charcoal, out-gassed at 1000° and placed in a salt solution in a vacuum, gave no hydrolytic adsorption. After exposure to oxygen, however, hydrolytic adsorption reappeared. The general change of hydrolytic adsorption with temperature of activation is as would be expected from the surface oxide theory, but there is one significant fact that the theory does not explain. The curves show that all three salts used gave no hydrolytic adsorption with a charcoal activated at 500°. A consideration of the relative adsorbability of benzoic acid, hydrochloric acid, and strong bases shows that the position of zero hydrolytic adsorption, *i.e.*, the position where acid and base are equally adsorbed, should be different for different salts. No explanation of the observed facts can be suggested.

## EXPERIMENTAL.

The charcoal used was prepared from "AnalaR" sucrose by charring it in a silica tube and heating it until no further fumes were evolved. After rough grinding, the charcoal was heated for 3 hours in a slow stream of carbon dioxide. No further attempt was made to purify the charcoal because such a purification involves treatment with hydrofluoric and hydrochloric acids, the last traces of which are extremely difficult to remove. The finely powdered charcoal was activated by 18 hours' heating in a silica tube furnace in a slow stream of moist oxygen (about 2 c.c. per minute). The temperature was measured by means of a thermocouple. After activation, the charcoal was removed from the furnace, tipped into a stoppered bottle, and quickly cooled.

The acid and base liberated during adsorption were estimated by electrometric titration with N/100-sodium hydroxide or hydrochloric acid, a glass electrode and a "Cambridge" valve electrometer being used. The titration vessel and electrodes were electrically shielded, and precautions against leakage currents were taken.

The total change in composition of the solutions was measured in order to obtain the molecular adsorption. Methylene-blue was estimated by titration with titanous sulphate, and chloride was estimated by Drechsel's modification of Volhard's method (*Z. anal. Chem.*, 1877, **16**, 351). A method for the estimation of benzoate similar to that of Henville (*Analyst*, 1927, **52**, 149) was used, except that the end-point was determined electrometrically with the glass electrode.

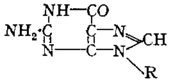
The following standard procedure was adopted for measuring the adsorption. 1—3 G. of charcoal were weighed into dry 6-oz. glass-stoppered bottles, and 150 c.c. of N/50-solutions of the various salts were run in. The bottles were vigorously shaken for a few minutes, and then left for 20 hours with occasional shaking. During the first stages of the adsorption, varying amounts of gas were evolved from the charcoal, especially from high-temperature samples. The solutions were filtered off through 7·0-cm. filter papers, and the first 10—15 c.c. of filtrate neglected; 100-c.c. portions of the filtrates were titrated with acid or alkali, and 25-c.c. portions were analysed to find the total adsorption. In general, the amount of acid or base in 100 c.c. of solution was equivalent to 0·5—8 c.c. of N/100-alkali or -acid. All the glass vessels were thoroughly steamed out before use. The solutions were kept as N/5-stock solutions, and diluted to the required strength immediately before use.

IMPERIAL COLLEGE OF SCIENCE, S.W. 7. [*Received, March 17th, 1938.*]

## 125. *Constitution of the Purine Nucleosides. Part VII. Guanosine and Guanine Deoxyriboside.*

By J. MASSON GULLAND and LEONARD F. STORY.

The method of determining the position of the carbohydrate radical in purine nucleosides (J., 1934, 1639; 1936, 765; 1937, 1912; this vol., p. 259) by comparing their ultra-violet absorption spectra with those of the corresponding 7- and 9-methylated purine derivatives has now been applied to guanosine, prepared from yeast nucleic acid, and to guanine deoxyriboside, obtained from thymus nucleic acid (Klein, *Z. physiol. Chem.*, 1933, **218**, 173). In both compounds (I), the carbohydrate radical has been shown to occupy position 9 for the reasons outlined below.

(I.) 

Guanosine, R = —CH·CH(OH)·CH(OH)·CH·$CH_2$·OH (—CH and ·CH— linked through O)

Guanine deoxyriboside, R = —CH·$CH_2$·CH(OH)·CH·$CH_2$·OH (—CH and ·CH— linked through O)

THE spectra of 7-methylguanine (Fischer, *Ber.*, 1897, **30**, 2400) (Fig. 2) and of 9-*methylguanine* (Fig. 1) are widely different in neutral and in alkaline solutions. The spectra of guanosine (Fig. 3) are scarcely to be distinguished from those of 9-methylguanine. This result confirms the placing of the carbohydrate radical in the 9-position by Gulland, Holiday, and Macrae (J., 1934, 1639) from a comparison of the spectra of xanthosine, prepared from guanosine, with those of 7- and 9-methylxanthines.

The spectra of guanine deoxyriboside in neutral and in alkaline solutions (Fig. 4) resemble those of 9-methylguanine and guanosine, but not those of 7-methylguanine. The spectrum of guanine deoxyriboside in acid solution has not been determined on account of the sensitivity of this substance to acid; Levene and Bass ("Nucleic Acids," p. 182, Chemical Catalog Co., New York) state that it is completely hydrolysed by 0·01N-sulphuric acid in 5 minutes.

### EXPERIMENTAL.

We are greatly indebted to Dr. W. Klein for a specimen of guanine deoxyriboside prepared from thymus nucleic acid by fission with nucleophosphatase from calf's intestinal mucosa.

Guanosine was prepared from guanylic acid, *ex* yeast nucleic acid, by hydrolysis with bone phosphatase (Gulland and Macrae, J., 1933, 662).

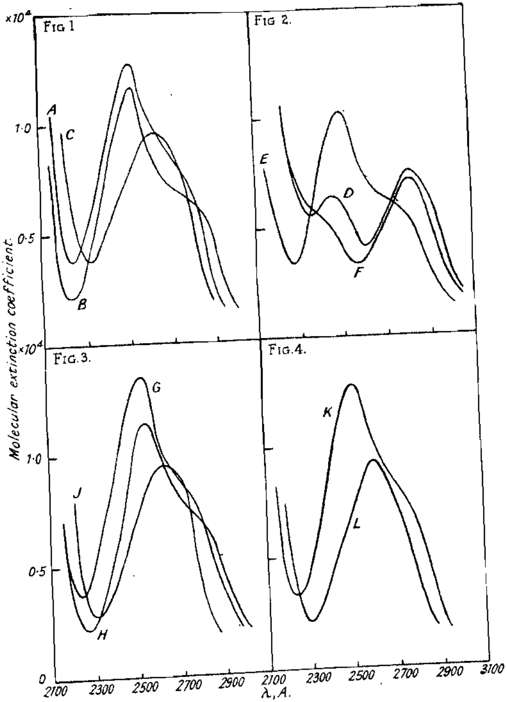



Fig. 1.

*9-Methylguanine*, M/50,000 : *A*, *in water*; *B*, *in* N/20-HCl; *C*, *in* N/20-NaOH.

Fig. 2.

*7-Methylguanine* : *D*, M/32,000 *in water*; *E*, M/44,000 *in* N/20-HCl; *F*, M/40,000 *in* N/20-NaOH.

Fig. 3.

*Guanosine*, M/50,000 : *G*, *in water*; *H*, *in* N/20-HCl; *J*, *in* N/20-NaOH.

Fig. 4.

*Guanine deoxyriboside*, M/50,000 : *K*, *in water*; *L*, *in* N/20-NaOH.

7-Methylguanine was prepared from theobromine through the stages of 2 : 6-dichloro-7-methylpurine and 2-chloro-6-hydroxy-7-methylpurine (Fischer, *Ber.*, 1897, **30**, 2400), and was purified by crystallisation of its hydrochloride from hydrochloric acid (*d* 1·07), decomposition of the hydrochloride by concentrated ammonium acetate, and crystallisation of 7-methylguanine in colourless needles from water (Found : N, 42·4. Calc. for $C_6H_7ON_5$ : N, 42·4%).

2 : 6-*Dichloro-9-methylpurine*. Violuric acid, prepared by the action of hydroxylamine on alloxan (Guinchard, *Ber.*, 1899, **32**, 1739), was reduced with hydrogen sulphide, and the resulting uramil was condensed with methyl *iso*thiocyanate to give 9-methylthiouric acid, which was converted into 9-methylxanthine by nitrous acid (Biltz and Strufe, *Annalen*, 1921, **423**, 200). A mixture of 9-methylxanthine (1 g.) and redistilled phosphorus oxychloride (40 g.) was heated at 180—190° for 20 hours in a sealed tube. The phosphorus oxychloride was removed under reduced pressure, ice added to the residue, and some unchanged 9-methylxanthine removed by filtration. When the filtrate was made alkaline with ammonia and then just acid with acetic acid, the crude 2 : 6-*dichloro-9-methylpurine* separated; after being extracted with cold dilute sodium hydroxide solution to remove a little soluble material, it crystallised from hot water in pale yellow, elongated prisms, m. p. 153° (Found : N, 27·6; Cl, 35·9. $C_6H_4N_4Cl_2$ requires N, 27·6; Cl, 35·0%).

9-*Methylguanine*.—The replacement of the chlorine in position 6 and the chlorine in position 2 of 2 : 6-dichloro-9-methylpurine by a hydroxyl and an amino-group respectively through successive treatment with sodium hydroxide and ammonia is inferred by analogy with the formation of 7-methylguanine from 2 : 6-dichloro-7-methylpurine by the same reactions in the same sequence.

Sodium hydroxide (0·25 g.) was added to 2 : 6-dichloro-9-methylpurine (0·6 g.) suspended in hot water (6 ml.), and the solution was shaken for 1 hour and acidified with acetic acid. The resulting 2-chloro-6-hydroxy-9-methylpurine, which crystallised from water in pale yellow prisms (decomp. at high temperature), was heated with 20 parts by vol. of aqueous ammonia (*d* 0·880) for 12 hours at 150—160° in a sealed tube. The solution was evaporated to dryness, and the residue washed with water to remove ammonium chloride, dissolved in dilute aqueous sodium hydroxide (norit), and acidified with acetic acid. Heating on the water-bath caused the formation of a voluminous crystalline mass of 9-methylguanine, which was purified by crystallising the hydrochloride in colourless oblique-ended prisms from hydrochloric acid (*d* 1·07), decomposing this with ammonium acetate, and recrystallising the product from water. 9-*Methylguanine* formed colourless rectangular plates, which decomposed at a high temperature without melting (Found : N, 42·3. $C_6H_7ON_5$ requires N, 42·4%). It dissolved readily in cold dilute hydrochloric acid and sodium hydroxide, was moderately soluble in hot water, slightly soluble in alcohol and chloroform, and insoluble in acetone.

*Absorption Spectra*.—Measurements were made with a Bellingham and Stanley quartz spectrograph No. 2 and photometer, the light source being a condensed spark between tungsten-steel electrodes. The solutions, prepared from dried materials and made to the strengths recorded on the Figs., were examined immediately in a layer thickness of 4 cm. against controls.

We acknowledge with pleasure our indebtedness to the Department of Scientific and Industrial Research for a maintenance grant (L. F. S.), and to the Chemical Society for a research grant.

UNIVERSITY COLLEGE, NOTTINGHAM. [Received, April 8th, 1938.]

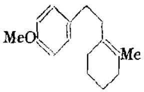
## 126. *Syntheses in the Phenanthrene Series. Part IX. 6-Methoxy-1-methylphenanthrene.*

By HAROLD PLIMMER, W. F. SHORT, and (in part) PETER HILL.

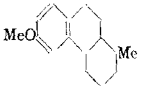
A synthesis of 6-*methoxy*-1-*methylphenanthrene* is described. The corresponding phenol is identical with the compound produced by the dehydrogenation of podocarpic acid.

IN attempting the synthesis of 6-*methoxy*-1-*methylphenanthrene* we first prepared 1-β-*p*-*anisylethyl-2-methyl*cyclo*hexene* (I) by employing methods similar to those recorded in Part V. Ring closure of this compound could yield the octahydrophenanthrenes (II) and (III) or the spiran (IV) (compare Harper, Kon, and Ruzicka, J., 1934, 125; Cohen, Cook, Hewett, and Girard, *ibid.*, p. 654; Hill, Short, and Stromberg, J., 1937, 1619). Successive treatment with aluminium chloride and sulphur afforded a liquid which furnished a picrate of somewhat indefinite melting point. Decomposition of the picrate produced an oil which on

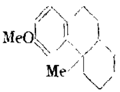
demethylation afforded a phenol, m. p. 104—108°. The properties and analyses of these compounds indicated that the dehydrogenation product consisted mainly of 3-methoxyphenanthrene.



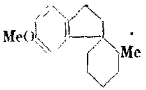
(I.)



(II.)

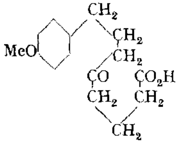


(III.)

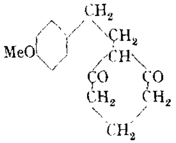


(IV.)

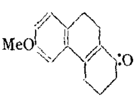
We then sought to obtain the desired phenanthrene by employing Robinson's hydrophenanthrene synthesis (J., 1935, 1288). γ-*p*-Anisylbutyryl chloride was condensed with ethyl sodio-α-acetylglutarate, and the product hydrolysed in stages to 5-*keto*-8-p-*anisyloctoic acid* (V). The yield was very small because the β-ketonic ester was mainly hydrolysed in the alternative direction. The *methyl* ester of (V) furnished β-p-*anisylethylcyclohexane*-2 : 6-*dione* (VI) when treated with sodium ethoxide in absolute ether, and dehydration with phosphoric oxide afforded 1-keto-6-methoxy-1 : 2 : 3 : 4 : 9 : 10-hexahydrophenanthrene (VII), which was characterised as its 2 : 4-*dinitrophenylhydrazone* m. p. 230—232°. The overall yield of this ketone was so poor that an alternative synthesis was sought.



(V.)

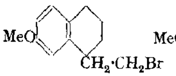


(VI.)

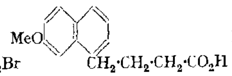


(VII.)

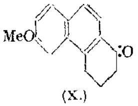
1-Keto-7-methoxy-1 : 2 : 3 : 4-tetrahydronaphthalene (Haworth and Sheldrick, J., 1934, 1951) was condensed with ethyl bromoacetate by the Reformatsky reaction to give ethyl 7-methoxy-3 : 4-dihydro-1-naphthylacetate, which on Bouveault–Blanc reduction afforded β-(7-methoxy-1 : 2 : 3 : 4-tetrahydro-1-naphthyl)ethyl alcohol (3 : 5-*dinitrobenzoate*, m. p. 119·5—120°). The corresponding *bromide* (VIII) was condensed with ethyl sodiomalonate, and the product hydrolysed, decarboxylated, and dehydrogenated with sulphur to γ-(7-*methoxy*-1-*naphthyl*)*butyric acid* (IX). The cyclic ketone (X) [2 : 4-*dinitrophenylhydrazone*, m. p. 261—262° (decomp.)] was obtained from the acid by the action of phosphoric oxide, and successive treatment with methylmagnesium iodide and sulphur afforded 6-*methoxy*-1-*methylphenanthrene* (XI), m. p. 87—87·5° (*picrate*, m. p. 140°). The corresponding *phenanthrol*, m. p. 161°, is identical with the dehydrogenation product of the resin acid podocarpic acid (forthcoming publication).



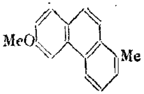
(VIII.)



(IX.)



(X.)



(XI.)

## EXPERIMENTAL.

β-p-*Anisylethyl Alcohol.*—The following modification of the method of Slotta and Heller (*Ber.*, 1930, **63**, 3029) gave a 50% yield of this alcohol. A solution of ethylene oxide (75·8 g.; 1·3 mols.) in dry benzene (200 c.c.) was added to an ice-cold Grignard solution prepared from magnesium (35 g.), *p*-bromoanisole (250 g.), and dry ether (1100 c.c.); dry toluene (440 c.c.) was then added and, after 60 hours, the mixture was distilled until the temperature reached 100°. The complex was decomposed in the usual way, and the product distilled. The alcohol had b. p. 145—147°/10 mm. and the fraction, b. p. 240—245°/10 mm., consisted of 4 : 4'-dimethoxydiphenyl, m. p.

171—173°. A 70% yield of *β-p-anisylethyl chloride*, b. p. 129·5—131°/10 mm., was obtained from the alcohol (93 g.), pyridine (75 c.c.), and thionyl chloride (54 c.c.) (Found: Cl, 20·7. $C_9H_{11}OCl$ requires Cl, 20·8%).

1-β-p-*Anisylethyl-2-methyl*cyclo*hexan-1-ol*.—The Grignard compound of the preceding chloride and 2-methyl*cyclo*hexanone afforded the tertiary *alcohol* as a viscous liquid, b. p. 173—175°/5 mm. (Found: C, 77·7; H, 9·8. $C_{16}H_{24}O_2$ requires C, 77·4; H, 9·7%), and dehydration with potassium hydrogen sulphate yielded 1-β-p-*anisylethyl-2-methyl*cyclo*hexene*, b. p. 156—156·5°/6 mm. (Found: C, 83·6; H, 9·4. $C_{16}H_{22}O$ requires C, 83·5; H, 9·6%). By the action of aluminium chloride on a solution of this compound in carbon disulphide, followed by dehydrogenation with sulphur at 180—240°, a viscous liquid was obtained. This gave an orange-red *picrate*, m. p. 114—116° after sintering at 95° (Found: C, 57·6; H, 3·6. $C_{16}H_{14}O,C_6H_3O_7N_3$ requires C, 58·5; H, 3·8%. $C_{15}H_{12}O,C_6H_3O_7N_3$ requires C, 57·7; H, 3·4%). Decomposition of the picrate with aqueous ammonia gave an oil, which on demethylation with hydrobromic–acetic acid afforded a *phenol*, m. p. 104—108° (Found: C, 86·2; H, 5·4. $C_{15}H_{12}O$ requires C, 86·5; H, 5·8%. $C_{14}H_{10}O$ requires C, 86·6; H, 5·15%). The m. p.'s recorded in the literature for 3-methoxyphenanthrene picrate and 3-hydroxyphenanthrene are 124—125° and 118—119° respectively.

*5-Keto-8-p-anisyloctoic Acid* (V).—β-4-Methoxybenzoylpropionic acid, prepared in 95% yield by the method of Fieser and Hershberg (*J. Amer. Chem. Soc.*, 1936, **58**, 2315), was reduced to γ-*p*-anisylbutyric acid as described by Haworth and Sheldrick (J., 1934, 1951). The average yield was 62% and it was usually unnecessary to purify the acid by esterification: a much lower yield was obtained by Martin's method (*J. Amer. Chem. Soc.*, 1936, **58**, 1438). The acid (70 g.) was converted into γ-*p*-anisylbutyryl chloride, which was carefully freed from thionyl chloride and dissolved in anhydrous ether (190 c.c.). The solution was slowly added below 15° to ethyl sodio-α-acetylglutarate (from 77·3 c.c. of the ester and 8·4 g. of powdered sodium) in dry ether (640 c.c.). After 59 hours at room temperature and 1 hour at the b. p. the mixture was added to ice-water and extracted with ether. The ethereal solution was washed with aqueous sodium carbonate (recovered *p*-anisylbutyric acid, 1·0 g.), dried, and evaporated. The residual liquid (134 g.) was shaken with 2·5% aqueous potassium hydroxide (3216 c.c.) for 17 hours, the strength of the alkali was then raised to 4%, and shaking continued for 4 hours. A small amount of undissolved ester was extracted with ether, and the aqueous solution acidified and extracted with ether. Evaporation of the ether left a brown oil, which was warmed on the steam-bath until evolution of carbon dioxide ceased and then heated with 2N-sodium hydroxide (432 c.c.) for 2 hours. The acids were liberated, extracted with ether, and esterified with a slight excess of diazomethane, and the esters fractionated. The following fractions were collected: (1) b. p. up to 160°/0·7 mm., mainly methyl γ-*p*-anisylbutyrate, and (2) b. p. 160—215°/0·7 mm. Fraction (2) solidified to a paste on cooling and, after removal of the solid, was redistilled, cooled, and filtered. These operations were repeated as long as solid fractions could be obtained. *Methyl 5-keto-8-p-anisyloctoate* separated from light petroleum (b. p. 40—60°) in white plates, m. p. 52° (Found: C, 69·2; H, 7·8. $C_{16}H_{22}O_4$ requires C, 69·1; H, 7·9%). The corresponding *acid* crystallised from light petroleum (b. p. 60—80°) in microscopic plates, m. p. 68° (Found: C, 68·1; H, 7·35. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·6%). The yield, calculated on the γ-*p*-anisylbutyric acid employed, was 8·5%.

β-p-*Anisylethyl*cyclo*hexane-2 : 6-dione* (VI).—Coarsely powdered sodium ethoxide (12 g.) was added to a solution of the preceding ester (6 g.) in dry ether (60 c.c.); the mixture was kept for 25 hours with occasional shaking and refluxed for ½ hour. Ice-water was then added, and neutral impurities removed from the alkaline solution by extraction with ether. The *dione*, liberated with cold dilute sulphuric acid, was collected in chloroform and recrystallised from light petroleum (b. p. 60—80°); it then had m. p. 167—169° (Found: C, 73·1; H, 7·3. $C_{15}H_{18}O_3$ requires C, 73·2; H, 7·3%). Yield, 47%.

1-*Keto-6-methoxy-1 : 2 : 3 : 4 : 9 : 10-hexahydrophenanthrene* (VII).—Phosphoric oxide (25 g.) was added in portions with stirring during 1½ hours to a boiling solution of the above dione (2·5 g.) in moist benzene (310 c.c.). The mixture was cooled, shaken with ice, made strongly alkaline, and extracted with ether. Acidification of the alkaline layer gave 0·2 g. of recovered dione. The benzene–ether solution was washed with water, dried, and evaporated in a vacuum. The residue (0·25 g.), which partly solidified, was characterised by its 2 : 4-*dinitrophenylhydrazone*. The red solid was purified by washing with alcohol, but could not be recrystallised; m. p. 230—232° (decomp.) (Found: C, 62·0; H, 5·05. $C_{21}H_{20}O_5N_4$ requires C, 61·8; H, 4·9%).

1-*Keto-7-methoxy-1 : 2 : 3 : 4-tetrahydronaphthalene*.—This ketone was obtained in 51% yield by the action of aluminium chloride on γ-*p*-anisylbutyryl chloride in tetrachloroethane solution

(Haworth and Sheldrick, *loc. cit.*). A good yield (up to 61%) of the ketone was obtained by adding phosphoric oxide (9 mols.) to a boiling solution of the acid in dry benzene, refluxing for 3 hours with mechanical stirring, and working up the product as described in previous parts of this series.

β-(*7-Methoxy-1 : 2 : 3 : 4-tetrahydro-1-naphthyl*)*ethyl Alcohol.*—A mixture of the cyclic ketone (1 mol.), zinc needles (1 atom), bromoacetic ester (1 mol.), dry benzene (5 c.c. per c.c. of ester), and a crystal of iodine was warmed at 60° until reaction set in and was then allowed to stand till the action ceased. After refluxing for ½ hour, the mixture was worked up in the known manner, and a benzene solution of the product refluxed for ½ hour with a little phosphoric oxide. The average yield of ester, b. p. 155—170°/0·8 mm., mostly at 165—167°/0·8 mm., was 67%. The ester (1 mol.) was dissolved in absolute alcohol (15 mols.) and reduced with sodium (7 atoms). A small amount of *7-methoxy-1 : 2 : 3 : 4-tetrahydro-1-naphthylacetic acid*, obtained from the alkaline layer, crystallised from aqueous methyl alcohol in white rectangular plates, m. p. 88—89° (Found : C, 70·9; H, 7·3. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%). The average yield of the alcohol, b. p. *ca.* 165°/0·4 mm., was 53% and the substance was characterised by its 3 : 5-*dinitrobenzoate*, which crystallised from ligroin in yellow needles, m. p. 119·5—120° (Found : C, 59·7; H, 5·1. $C_{20}H_{20}O_7N_2$ requires C, 60·0; H, 5·0%). A mixture of phosphorus tribromide (4 c.c.) and chloroform (24 c.c.) was slowly added to a mechanically stirred ice-cold solution of the alcohol (23·3 g.) in chloroform (58 c.c.), and the β-(*7-methoxy-1 : 2 : 3 : 4-tetrahydro-1-naphthyl*)*ethyl bromide*, b. p. 155—160°/0·4 mm., isolated in the usual way (Found : Br, 29·1. $C_{13}H_{17}OBr$ requires Br, 29·7%). Average yield, 64·5%.

γ-*7-Methoxy-1-naphthylbutyric Acid* (IX).—A solution of the preceding bromide (1 mol.) in dry toluene (1 c.c. per g.) was slowly added at room temperature to ethyl potassiomalonate (from the metal, 1·7 atoms; ethyl malonate, 2 mols.; toluene, 13·0 c.c. per g. of metal), and the mixture heated at 120—130° for 68 hours and worked up in the usual way. The ethyl β-(7-methoxy-1 : 2 : 3 : 4-tetrahydro-1-naphthyl)ethylmalonate was obtained in 82% yield as a viscous liquid, b. p. 220—230°/0·6 mm.; reduction in the amount of malonic ester resulted in a greatly diminished yield. Hydrolysis of the ester afforded the acid as a viscous liquid, which was decarboxylated at 120—200°. The resulting γ-(7-methoxy-1 : 2 : 3 : 4-tetrahydro-1-naphthyl)butyric acid (yield, 79%) would not crystallise and was therefore heated at 215—230° for 5 hours with ½ of its weight of sulphur. The residual black mass was repeatedly extracted with warm dilute aqueous sodium hydroxide; the solution was filtered, extracted with ether, and acidified. The acid was collected and purified by solution in dilute aqueous sodium carbonate and recrystallisation from methyl alcohol. γ-*7-Methoxy-1-naphthylbutyric acid* crystallised in long rods, m. p. 105—106° (Found : C, 73·5; H, 6·5. $C_{15}H_{16}O_3$ requires C, 73·8; H, 6·6%). Yield, 34%.

*1-Keto-6-methoxy-1 : 2 : 3 : 4-tetrahydrophenanthrene* (X).—Ring closure was effected by addition of phosphoric oxide (20 g.) to a solution of the butyric acid (3 g.) in boiling benzene (45 c.c.) as previously described and the cyclic ketone was isolated in 83% yield as a glassy mass. The 2 : 4-*dinitrophenylhydrazone* crystallised from boiling benzene in bright red, stout needles, m. p. 261—262° after sintering at 256° (Found : C, 61·9; H, 4·6. $C_{21}H_{18}O_5N_4$ requires C, 62·1; H, 4·4%).

*6-Methoxy-1-methylphenanthrene* (XI).—An ethereal solution of the cyclic ketone (1 mol.) was added to an ice-cold solution of methylmagnesium iodide (3 mols.), and the mixture refluxed for 6 hours and worked up in the known manner. The crude condensation product (yield, 80%) was treated at 180—250° for 5 hours with sulphur (1 atom) and distilled in a vacuum. The viscous brown distillate was warmed with excess of alcoholic picric acid, and the crude picrate pressed on porous tile and decomposed with warm aqueous ammonia. The oily globules solidified on cooling and were washed with water until free from ammonium picrate. Successive crystallisation from methyl alcohol (charcoal) and light petroleum (b. p. 40—60°) gave cream-coloured clustered needles of *6-methoxy-1-methylphenanthrene*, m. p. 87—87·5° (Found : C, 86·6; H, 6·4. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). The *picrate* consisted of vermilion needles, m. p. 140—141·5° (Found : C, 58·4; H, 3·8. $C_{16}H_{14}O,C_6H_3O_7N_3$ requires C, 58·5; H, 3·8%). Demethylation of the methyl ether with hydrobromic–acetic acid afforded *6-hydroxy-1-methylphenanthrene*, which crystallised from chloroform in white plates, m. p. 161° (Found : C, 86·4; H, 6·0. $C_{15}H_{12}O$ requires C, 86·5; H, 5·8%).

We are grateful to the Chemical Society for a grant.

THE COLLEGE OF TECHNOLOGY, MANCHESTER. [*Received, March 24th*, 1938.]

## 127. *Reduction of the Carbonyl Group in Unsaturated Ketones, and the Interconversion of Geometrical Isomerides during such Reduction.*

By C. L. Arcus and J. Kenyon.

The uusaturated ketone *n*-butylideneacetone is reduced by aluminium *iso*propoxide to α-methyl-γ-*n*-propylallyl alcohol without simultaneous etherification or reduction of the double bond. Since both the *cis*- and the *trans*-form of the ketone yield identical products, this reagent appears to facilitate interconversion of geometrical isomerides.

During an experimental study of the reactions of *n*-propylpropenylcarbinol (Arcus and Kenyon, this vol., p. 312), the preparation of dl-*α-methyl-γ-*n*-propylallyl alcohol* (I) became

(I.) $CHPr^{a}:CH\cdot CHMe\cdot OH$ . $CHPr^{a}:CH\cdot COMe$ (II.)

desirable. It has now been prepared by the reduction of *n*-butylideneacetone (II), the *cis*- and *trans*-forms of which were described by Eccott and Linstead (J., 1930, 905). The *cis*-form was prepared by condensing *n*-butaldehyde with acetone and allowing the (exothermic) reaction to proceed unchecked. The slow addition of *n*-butaldehyde to a cooled mixture of acetone and alkali yields the ketol $CHPr^{a}(OH)\cdot CH_2\cdot COMe$, which, on dehydration with anhydrous oxalic acid gives the *trans*-form of (II). These isomerides have different physical constauts and yield different semicarbazones.

Reduction was effected with a solution of aluminium *iso*propoxide in *iso*propyl alcohol by the Ponndorf–Meerwein method (Meerwein and Schmidt, *Annalen*, 1925, **444**, 221;

$$COR_1R_2 + CHMe_2\cdot O\cdot al \rightleftharpoons COMe_2 + CHR_1R_2\cdot O\cdot al$$

Ponndorf, *Z. angew. Chem.*, 1926, **39**, 138): Lund (*Ber.*, 1937, **70**, 1520) has shown that, by this method, unsaturated ketones yield mainly the *iso*propyl ethers of the unsaturated alcohols initially produced. In the present instance the reaction was stopped as soon as the evolution of acetone had markedly diminished, and although some polymerisation was observed, neither the *iso*propyl ether nor the saturated alcohol was encountered.

From the product of reduction of the *cis*- and of the *trans*-isomeride of the ketone it was possible in each case to isolate—by means of the hydrogen phthalic ester—only one, and the same, alcohol. Since Eccott and Linstead (*loc. cit.*) found the isomeric ketones strongly resistant to configurative change and to yield high-boiling products with alkaline catalysts, it appears very probable that interconversion of geometrical isomerides occurs at the stage when the alcohols exist as aluminium alkoxides.

The identity of α-methyl-γ-*n*-propylallyl alcohol was demonstrated by catalytic reduction to methyl-*n*-amylcarbinol.

### Experimental.

*Reduction of* cis-n-*Butylideneacetone*.—The crude ketone, b. p. 71—77°/16 mm., prepared by the method of Eccott and Linstead (*loc. cit.*), was dried by addition of an equal volume of dry benzene and removal of the latter by distillation through a column; the remaining ketone had b. p. 80°/27 mm. By the special procedure of Eccott and Linstead it furnished a semicarbazone having, after three recrystallisations from aqueous alcohol, m. p. 155°.

This material (132 g.) was added to a solution of aluminium *iso*propoxide in *iso*propyl alcohol (3N, 620 c.c.; prepared by the procedure of Lund, *loc. cit.*), and the mixture heated on a steam-bath in a flask fitted with a return condenser through which water at 65—70° was circulated; acetone distilled over, but the *iso*propyl alcohol was returned. After 4 hours the excess of *iso*propyl alcohol was removed under diminished pressure, and the residue decomposed with ice and dilute sulphuric acid. From an ethereal extract, washed, and dried with potassium carbonate, the crude alcohol, b. p. 69°/17 mm., was obtained. This (39 g.) was heated with a suspension of phthalic anhydride (51 g.) in pyridine (27 g.) at 60—70° for 2 hours, and the cooled product extracted with dilute aqueous ammonia. Extraction of the acidified ammoniacal solution with ether yielded a crystalline product (73 g.), which after two crystallisations from light petroleum gave dl-*α-methyl-γ-*n*-propylallyl hydrogen phthalate* in needles, m. p. 67° (Found, by titration with NaOH: *M*, 262. $C_{15}H_{18}O_4$ requires *M*, 262).

dl-α-*Methyl-γ-*n-*propylallyl alcohol.* Steam was passed through a solution of the hydrogen phthalic ester (16 g.) and sodium hydroxide (5·4 g.) in water (27 c.c.); extraction of the distillate yielded the *alcohol*, b. p. 66—67°/16 mm., $n_D^{18°}$ 1·4391, $d_{4°}^{17°}$ 0·834 (Found: C, 73·8; H, 12·4. $C_7H_{14}O$ requires C, 73·6; H, 12·4%). Its p-*nitrobenzoate*, formed by adding *p*-nitrobenzoyl chloride (1·6 g.) to a solution of the alcohol (1·0 g.) in pyridine (0·7 g.) and after an interval heating the mixture at 60° for an hour, separated from light petroleum in plates, m. p. 29·5° (Found: C, 64·6; H, 6·6. $C_{14}H_{17}O_4N$ requires C, 63·8; H, 6·5%). Its p-*xenylurethane*, prepared by heating a mixture of the alcohol (1·2 g.) with *p*-xenylcarbimide (2·0 g.) on the steam-bath for an hour, separated from ether–light petroleum in needles, m. p. 87° (Found: C, 77·4; H, 7·35. $C_{20}H_{23}O_2N$ requires C, 77·7; H, 7·5%).

*Reduction of* trans-n-*Butylideneacetone.*—The ketol (heptan-δ-ol-β-one), prepared according to Eccott and Linstead (*loc. cit.*), b. p. 99°/15 mm., was dehydrated with anhydrous oxalic acid, and the resulting *trans-n*-butylideneacetone, b. p. 61—63°/12 mm., dried by the method described above. It furnished, by the procedure indicated above, a semicarbazone having, after three recrystallisations, m. p. 126°, not increased by further recrystallisation. This material (160 g.), reduced in the same manner as the *cis*-isomeride, yielded the crude alcohol, b. p. 64°/14 mm. This was converted into its hydrogen phthalic ester (100 g.) which, after recrystallisation from light petroleum, formed needles, m. p. 67° alone or when mixed with the hydrogen phthalate of the alcohol obtained by the reduction of the corresponding *cis*-ketone.

*Reduction of* dl-α-*Methyl-γ-*n-*propylallyl Alcohol to* dl-*Methyl*-n-*amylcarbinol.*—The alcohol (3·3 g.) in ether (24 c.c.) was reduced with hydrogen at 2 atm., in the presence of the platinum catalyst of Adams, Voorhees, and Shriner ("Organic Syntheses," **8**, 92). The solution yielded *dl*-methyl-*n*-amylcarbinol, b. p. 64—65°/13 mm., $n_D^{17°}$ 1·4226; the hydrogen phthalate had m. p. 57·5° (Pickard and Kenyon, J., 1911, **99**, 45, recorded b. p. 73·5°/20 mm., $n_D^{20°}$ 1·4209; *dl*-hydrogen phthalic ester, m. p. 57—58°).

Thanks are expressed to the Government Grants Committee of the Royal Society and to Imperial Chemical Industries, Ltd., for grants; one of us thanks the Department of Scientific and Industrial Research for the award of a maintenance grant.

BATTERSEA POLYTECHNIC, LONDON, S.W. 11. [*Received, March 14th, 1938.*]

## 128. *Union of Aryl Nuclei. Part III. 3'-Hydroxy-*meso*benzanthrone.*

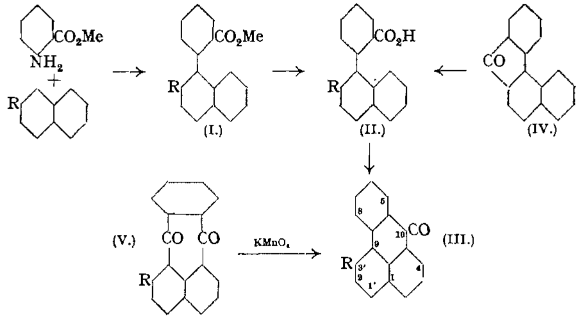
By I. M. HEILBRON, D. H. HEY, and R. WILKINSON.

The extension of the Gomberg reaction to include the use of solid reactants in solution (as shown in Part I) is applied to the reaction between diazotised methyl anthranilate and a solution of 2-methoxynaphthalene in chloroform. The product, *methyl 2-methoxy-1-phenylnaphthalene-2'-carboxylate*, is converted, by the action of aluminium chloride on the acid chloride, into 3'-hydroxy*meso*benzanthrone, which is methylated to give *3'-methoxy*meso*benzanthrone.* The hydroxybenzanthrone thus obtained is identical with that prepared by the oxidation of 1 : 8-phthaloyl-2-naphthol with permanganate.

IN Part I (this vol., p. 108) it was shown that the method for the synthesis of biaryl compounds due to Gomberg and his co-workers (*J. Amer. Chem. Soc.*, 1924, **46**, 2339; 1926, **48**, 1372) could be extended to include the use of solid reactants dissolved in a suitable solvent; *e.g.*, from diazotised methyl anthranilate and a solution of naphthalene in carbon tetrachloride, methyl *o*-α-naphthylbenzoate (I, R = H) was obtained. The free acid (II, R = H) derived from this ester was converted by ring closure into *meso*benzanthrone (III, R = H), a reaction which had been carried out previously by Schaarschmidt and Georgeacopol (*Ber.*, 1918, **51**, 1085), who obtained their acid, however, by the alkaline fusion of 3 : 4-benzfluorenone (IV).

Since the yield of the naphthylbenzoic ester (I, R = H) was low and some of the diazo-compound from the methyl anthranilate obviously reacted with the solvent with formation of methyl *o*-chlorobenzoate, a more reactive component was sought and the present

communication deals with the reaction between diazotised methyl anthranilate and 2-methoxynaphthalene.




In the reaction between diazotised methyl anthranilate and naphthalene there was no indication of condensation at the β-positions in the naphthalene molecule. It is now shown that in the case of 2-methoxynaphthalene condensation takes place to a preponderating extent at position 1, giving rise to *methyl 2-methoxy-1-phenylnaphthalene-2′-carboxylate* (I, R = OMe), which on ring closure by the action of aluminium chloride on the acid chloride yields 3′-hydroxy*meso*benzanthrone (III, R = OH). Methylation with methyl iodide or methyl sulphate gives *3′-methoxy*meso*benzanthrone* (III, R = OMe). The yield of the ester (I, R = OMe) from 2-methoxynaphthalene was approximately 20%, calculated on the weight of methyl anthranilate. Chloroform was used throughout as solvent, since it appeared to react with the diazo-compound to a smaller extent than did carbon tetrachloride.

A compound stated to be 3′-hydroxy*meso*benzanthrone (III, R = OH) was obtained by Rieche, Sauthoff, and Müller (*Ber.*, 1932, **65**, 1371) from the oxidation of 1 : 8-phthaloyl-2-naphthol (V, R = OH) with potassium permanganate. The constitution of the phthaloyl-β-naphthol, which was obtained from the condensation of phthalic anhydride with β-naphthol in the presence of sulphuric acid (Rieche and Frühwald, *Ber.*, 1931, **64**, 1603) or aluminium chloride (Fieser, *J. Amer. Chem. Soc.*, 1931, **53**, 3546), was questioned by Fieser (*loc. cit.*), but later accepted (*ibid.*, 1933, **55**, 3010). The manner in which 3′-hydroxy*meso*-benzanthrone is obtained on oxidation, however, remains somewhat obscure, but there can now be little doubt about the constitution of this compound, since a repetition of the permanganate oxidation of the phthaloyl-β-naphthol yielded a product identical with that obtained from the methoxynaphthylbenzoic acid (II, R = OMe) resulting from the Gomberg reaction. In addition the preparation of 3′-hydroxy*meso*benzanthrone by the oxidation of 1 : 8-phthaloyl-2-naphthol with alkaline potassium ferricyanide has also been described (I.G., D.R.P. 555,938), and the product is stated to be identical with that obtainable from 7-hydroxy-1-benzoylnaphthalene.

## EXPERIMENTAL.

*2-Methoxy-1-phenylnaphthalene-2′-carboxylic Acid* (II, R = OMe).—Molten methyl anthranilate (50 g.) was poured with rapid stirring into dilute hydrochloric acid (83 c.c., *d* 1·16, in 40 c.c. of water) and the resulting fine paste was diazotised in the normal manner with aqueous sodium nitrite (25 g. in 40 c.c.). Aqueous sodium hydroxide (30 g. in 100 c.c.) was added gradually to a vigorously stirred mixture of the diazonium solution and a solution of 2-methoxynaphthalene (100 g., prepared by the method of Hiers and Hager, " Organic Syntheses," IX, p. 13) in chloroform (400 c.c.) at 0—5°. Stirring was continued for about 12 hours, during which the temperature was gradually raised to 25°. The chloroform layer was separated, washed with hydrochloric acid

and with water, dried over sodium sulphate, and distilled. The excess of 2-methoxynaphthalene was recovered at 130—150°/15 mm. and crude methyl 2-methoxy-1-phenylnaphthalene-2′-carboxylate was collected at 185—195°/15 mm. as a pale yellow oil, leaving a considerable quantity of high-boiling tar. The ester was boiled under reflux with 20% alcoholic potassium hydroxide, and the solution poured into water, filtered from impurities, and acidified with hydrochloric acid. The precipitated acid (17 g.) was boiled in alcoholic solution (charcoal), repeatedly crystallised from the same solvent, sublimed in a high vacuum, and finally crystallised from absolute alcohol, giving fine colourless needles of *2-methoxy-1-phenylnaphthalene-2′-carboxylic acid*, m. p. 218—220° (Found : C, 77·6; H, 5·3. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·0%). The *methyl* and the *ethyl* ester, prepared by the Fischer–Speier method, had m. p. 85—86° (Found : C, 78·4; H, 5·3. $C_{19}H_{16}O_3$ requires C, 78·1; H, 5·5%) and 83—84° (Found : C, 78·6; H, 6·1. $C_{20}H_{18}O_3$ requires C, 78·4; H, 5·9%), respectively.

Reactions were also carried out (a) with 60% sulphuric acid and solid sodium nitrite, (b) at temperatures varying from 0° to 25°, and (c) with carbon tetrachloride as solvent, but no improvement in yield resulted.

3′-*Hydroxy*meso*benzanthrone* (III, R = OH).—A mixture of 2-methoxy-1-phenylnaphthalene-2′-carboxylic acid (3 g.), dry benzene (40 c.c.), and phosphorus pentachloride (2·3 g.) was boiled under reflux for ½ hour. Finely powdered aluminium chloride (7 g.) was added to the cold mixture, which was then heated at 60° for 2½ hours. The product was poured into water, the benzene removed in steam, the residual brownish solid extracted with aqueous sodium carbonate, and the filtered extract acidified with hydrochloric acid. The precipitated 3′-hydroxy*meso*benzanthrone sublimed in a high vacuum as a bright orange-yellow powder, m. p. 290—292° (Found : C, 82·6; H, 4·15. Calc. for $C_{17}H_{10}O_2$: C, 82·9; H, 4·1%) (cf. Rieche, Sauthoff, and Müller, *loc. cit.*).

3′-*Methoxy*meso*benzanthrone* (III, R = OMe).—A mixture of 3′-hydroxy*meso*benzanthrone (1 g.), methyl iodide (0·6 g.), and potassium carbonate (0·3 g.) was boiled under reflux with acetone (50 c.c.) for 10 hours. After removal of the acetone by distillation, the residue was boiled with water. The yellow insoluble residue (1 g.), on sublimation in a high vacuum, yielded 3′-*methoxy*meso*benzanthrone* as a light yellow powder, m. p. 147—148° (Found : C, 82·5; H, 4·8. $C_{18}H_{12}O_2$ requires C, 83·1; H, 4·6%).

1 : 8-*Phthaloyl-2-naphthol* (V, R = OH).—Two methods of preparation were used, both of which gave low yields. (i) A mixture of β-naphthol (20 g.), phthalic anhydride (20 g.), boric acid (20 g.), and concentrated sulphuric acid (100 c.c.) was heated with stirring at 160° for 6 hours (cf. Rieche and Frühwald, *loc. cit.*). The solution was poured on ice; the yellow precipitate, after being washed with water (yield 4 g.) and sodium carbonate solution and crystallised from glacial acetic acid, had m. p. 195—196°. (ii) When β-naphthol (15 g.) had been added gradually to a fused mass of phthalic anhydride (250 g.) and aluminium chloride (100 g.), the mixture became too stiff to stir even at 250°. The solidified melt was crushed, and the phthaloyl-β-naphthol (8 g.) isolated as described above (cf. Bayer and Co., D.R.P. 298,345; Fieser, *J. Amer. Chem. Soc.*, 1931, **53**, 3546; Rieche, Sauthoff, and Müller, *loc. cit.*).

*Oxidation of* 1 : 8-*Phthaloyl-2-naphthol.*—An aqueous solution of potassium permanganate (5 g.) was added during 6 hours to a stirred solution of 1 : 8-phthaloyl-2-naphthol (7 g.) in aqueous sodium hydroxide (23 g. in 280 c.c.) heated on the water-bath. Stirring and heating were continued for a further 2 hours, and the solution then cooled, filtered, and acidified. The yellow precipitate was washed and extracted repeatedly with aqueous sodium bicarbonate. Acidification of the extracts precipitated 3′-hydroxy*meso*benzanthrone as a yellow powder. After purification by sublimation it melted at 290°, both alone and on admixture with the specimen prepared from the methoxynaphthylbenzoic acid. The methyl ethers of the two specimens also showed no depression of m. p.

The authors' thanks are due to Dr. J. L. Dunn and Dr. W. S. M. Grieve for assistance with preliminary work, and to Imperial Chemical Industries Ltd. (Dyestuffs Group) for grants and gifts of chemicals.

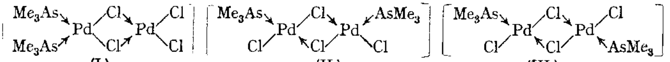
The University, Manchester. [*Received, March 28th,* 1938.]

# 129. *The Constitution of Complex Metallic Salts. Part VII. The Structure and Configuration of the Bridged Derivatives of Trimethylarsine with Palladous Halides.*

By Frederick G. Mann and Alexander F. Wells.

It has previously been shown that the bridged derivatives of the trialkyl-phosphines and -arsines with palladous halides, *e.g.*, $[R_3P,PdCl_2]_2$ and $[R_3As,PdCl_2]_2$, exist in the solid state as only one of the three theoretically possible isomeric forms (I—III below): in organic solvents all three forms are apparently present in tautomeric equilibrium. Crystallographic examination of the isomorphous trimethylarsine members, $[Me_3As,PdCl_2]_2$ and $[Me_3As,PdBr_2]_2$, proves that these compounds have a planar molecule with a centre of symmetry, and must therefore be the isomer (III). The dimensions of these molecules and their orientation in the crystal have been determined. The significance of these results is discussed.

In Part IV (Mann and Purdie, J., 1936, 873) the constitution of the trialkyl-phosphine and -arsine derivatives of various palladous salts, having the molecular formulæ $[R_3P,PdX_2]_2$ and $[R_3As,PdX_2]_2$ where X is a univalent acid radical, was discussed, and a considerable volume of evidence was adduced to show that in these compounds the two palladium atoms are linked or "bridged" through two acid radicals. It followed that the trimethylarsinepalladous chloride member, $[Me_3As,PdCl_2]_2$, for example, should theoretically exist in three isomeric forms, *viz.*, the unsymmetrical form (I), and the *cis*- and *trans*-members of the symmetrical form (II and III, respectively). It was shown, however,



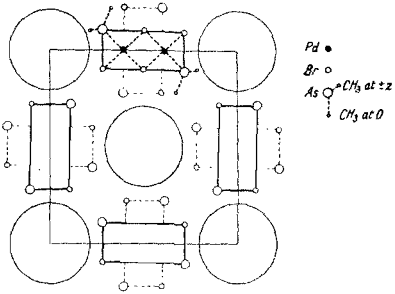
(I.) (II.) (III.)

that such isomerism did not apparently occur in the solid state, since each compound examined was crystallographically homogeneous and (except the lower homologous members) of sharp melting point. Moreover, the *n*-butylphosphine and the *n*-butylarsine members were isomorphous, and therefore the two homologous series had identical structures in the solid state. In organic solvents, however, these compounds gave a number of reactions indicating clearly the existence of both the unsymmetrical (I) and the symmetrical (II and III) forms, and it followed that in such solutions these isomeric forms exist apparently in tautomeric equilibrium.

In order to determine which of the three isomeric forms exists in the solid state, a crystallographic examination has now been made of dichlorobis(trimethylarsine)-$\mu$-dichlorodipalladium (I—III) and of the analogous bromine *compound* $[Me_3As,PdBr_2]_2$. These compounds were selected because it was essential to examine the first member of the homologous series in order to minimise complications caused by the alkyl groups: furthermore, the methylarsine derivatives were more readily accessible than the methylphosphine derivatives, and the arsenic atom more suitable for *X*-ray detection than the lighter phosphorus atom. (For investigation of the reactions of this class of compound in solution, the butyl members were earlier used because of their higher solubility and greater thermal stability.) The tetrachloride and the tetrabromide were obtained from various solvents as very fine needles: the best-developed crystals were obtained in each case from dioxan, from which the two compounds separated as isomorphous tetragonal prisms. A complete *X*-ray examination has been made of the tetrabromide. It was first established that the molecules—apart from the alkyl groups—are planar (in accordance with formulæ I—III) and that the crystals are built up of parallel layers of such molecules. The molecule, furthermore, possesses a diad axis of symmetry perpendicular to the plane of the molecule and therefore must have the *trans*-symmetrical structure such as (III). The orientation of the molecules in the crystal was then determined: this is depicted diagrammatically in Fig. 1, which shows the relative position of four such molecules in

one plane, and that of the corresponding four molecules in the plane below. The relative position of the atoms in the molecule was finally determined (Fig. 2), and conclusive

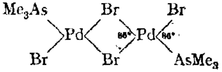
Fig. 1.




*Projection of the structure of* $[Me_3As,PdBr_2]_2$ *on* (001)*—diagrammatic. Molecules at* z = 0 *are distinguished by heavy unbroken lines, those at* $z = \frac{1}{2}$ *by light dotted lines. The heavy dotted lines indicate the bonds in one molecule at* z = 0; *the palladium atoms and the bridged bromine atoms are shown in this molecule only. The large circles* (*radius* 3·45 A.) *represent the possible position of dioxan molecules.*

proof of the *trans*-symmetrical formula thus obtained. The palladium atoms are therefore definitely bridged by bromine atoms, and the four-membered ring thus produced has an angle of 86° at the palladium atoms: the opposite angle in each case, between the arsenic-palladium-bromine atoms, has the same value. The distance between the palladium atoms and neighbouring bromine atoms (bridged and unbridged) has a constant value, 2·45 A., that between palladium and neighbouring arsenic atoms being slightly greater, 2·50 ± 0·05 A.

Fig. 2.

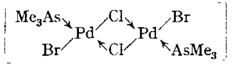


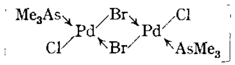

*Configuration and dimensions of the dibromobis(trimethylarsine)-μ-dibromodipalladium molecule.*
*Interatomic distances:* Pd–Br, 2·45 A.; Pd–As, 2·50 ± 0·05 A.

An interesting point arose in connexion with the purification of these compounds. When the tetrachloride and tetrabromide were recrystallised from alcohol, the fine needles, when dried in a vacuum desiccator for 3—4 hours, were pure. When these compounds were recrystallised from dioxan, similar but larger and better-formed needles were obtained, which however usually still contained traces of dioxan even after 24 hours in a vacuum desiccator. These last traces of dioxan were then slowly lost in the desiccator (most rapidly from the smallest crystals), but the crystal form and structure of the compounds were unaffected by this loss of solvent: hence the dioxan could not have been originally chemically combined with the palladium molecule. The explanation of this phenomenon is that the orientation of the molecules in the crystal (Fig. 1) gives rise to cylindrical tunnels in the crystal parallel to the *c* axis, *i.e.*, at right angles to the layers of the planar molecules. The molecules of a solvent (if not too large) may therefore occupy these tunnels without appreciable distortion of the crystal structure, such molecules having clearly no linkage or constant proportion to the palladium molecules. The comparatively small and readily volatile molecules of alcohol are quickly lost from these tunnels when the crystals are placed in a vacuum. The cyclic molecules of dioxan have a diameter approximating to that of these tunnels, and the escape of these larger and less volatile molecules must obviously be a much slower process. The growth of the crystals in dioxan does, however, cause a slight change in the cell dimensions: thus the needles of the tetrachloride from alcohol and dioxan are isomorphous, but the needles from dioxan have cell dimensions 1·5% greater than those of the needles from alcohol. This movement

of solvent molecules through tunnels in the crystal structure is not a novel phenomenon, and this example is probably closely parallel to that of the water molecules in the zeolite crystals.

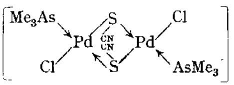
Since the configuration of these bridged palladium compounds was thus accurately known, it was of interest to investigate a similar compound having mixed acid radicals, and for this purpose the *dichloride-dibromide* compound, $[Me_3As,PdClBr]_2$, was prepared; it was obtained by the action of ammonium palladochloride on *dibromobis(trimethylarsine)-palladium*, $[(Me_3As)_2PdBr_2]$, and separated readily from alcohol in needles very similar to, but not isomorphous with, those of the tetrachloride and tetrabromide. After this main crop had been removed, the mother-liquor on standing deposited small quantities of compact monoclinic crystals; when these crystals were collected, the disturbance of the solution owing to the filtration caused the more rapid separation of fine rhombic needles. Three forms of this compound were thus obtained. The rhombic needles contained 8 molecules of $[Me_3As,PdClBr]_2$ in the cell and were therefore not further investigated. The monoclinic crystals, however, had only 2 molecules in the cell and these molecules possessed a centre of symmetry: they must therefore have the structure (IV) or (V), and are of the same isomeric form as the tetrachloride and tetrabromide. The re-

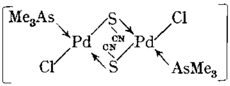
(IV.) 


 (V.)


actions of the tributylphosphine dichloride-dibromide, $[Bu_3{}^{a}P,PdClBr]_2$, which have been studied and will be described in a subsequent communication, give strong evidence that the bridging in this molecule is through the bromine atoms, and by analogy it is probable that the monoclinic crystals of the trimethylarsine compound have the structure (V). It should be noted, however, that each of the three isomeric forms of the trimethylarsine tetrachloro-compound (I, II, and III) can theoretically give rise to four isomeric compounds when two of the four chlorine atoms are replaced by bromine, and the dichloride-dibromide may be formulated therefore in twelve isomeric forms.

Other mixed compounds of this type, such as the *dichloride-dithiocyanate*, $[Me_3As,PdCl(SCN)]_2$ (VI), and the *dibromide-dithiocyanate*, $[Me_3As,PdBr(SCN)]_2$, have now been prepared for investigation. These two compounds were obtained by the action of ammonium palladochloride and palladobromide respectively on *dithiocyanatobis(trimethylarsine)palladium*, $[(Me_3As)_2Pd(SCN)_2]$, and it is known (Mann and Purdie, *loc. cit.*)

(VIA.) 

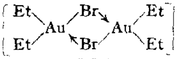

 (VIB.)

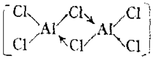

that in such compounds the palladium atoms are bridged through the thiocyanate groups. An additional cause of isomerism will arise in such compounds, however, as the tetrahedral disposition of the co-ordinated sulphur atoms will cause the — CN groups to adopt either the *cis-* or the *trans*-position (VIA and VIB respectively) relative to the plane of the molecule.

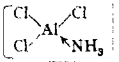
*Dichlorobis(trimethylphosphine)-μ-dichlorodipalladium*, $[Me_3P,PdCl_2]_2$, has also been prepared for crystallographic investigation; it separates as large, well-formed, monoclinic crystals, which are therefore not isomorphous with those of the trimethylarsine analogue. The fact that, in the homologous phosphine and arsine palladium compounds, isomorphism is not shown by the methyl members but is shown by the *n*-butyl members is not surprising, since as each series is ascended the effect of the six increasingly large alkyl groups will tend more and more to minimise the difference in the inorganic portion of the molecules.

This elucidation of the structure of the tetrachloride and tetrabromide, together with the fact that Burawoy, Gibson, Hampson, and Powell (J., 1937, 1690) have found a similar structure for diethylmonobromogold (VII), gives decisive proof of the existence of the

bridged linking of metallic atoms through acid radicals and other similar groups, a type of linking first used in 1905 by Werner ("Neuere Anschauungen auf dem Gebiete der Anorganischen Chemie," 1st edtn., pp. 63, 71, 188), who later extended its use considerably *

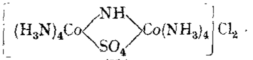

(VII.)

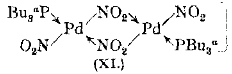

(VIII.)


(IX.)

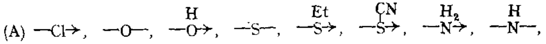
(*op. cit.*, 2nd edtn., 1909, p. 185 *et seq.*). There is little doubt that this type of linking is commoner than has been supposed, and that it exists, not only in compounds such as $[CO,PtCl_2]_2$ and $[C_2H_4,PtCl_2]_2$, but also in several volatile metallic chlorides which exhibit immediately above their boiling point a vapour density corresponding to a bimolecular form. Chief among the latter are aluminium chloride (VIII) (Werner, *op. cit.*, 5th edtn., 1923, p. 285), gallium trichloride, and ferric chloride. The bridged linkage in these metallic chlorides is clearly not of great stability, since at higher temperatures the vapour density falls to that required for the unassociated chloride; for instance, the density of aluminium chloride vapour corresponds at 430° to $Al_2Cl_6$ and at 800° to $AlCl_3$, similar results being obtained for ferric and gallium chlorides (Friedel and Crafts, *Compt. rend.*, 1888, **106**, 1764; **107**, 301, 306; Nilson and Pettersson, *Z. physikal. Chem.*, 1889, **4**, 222; Biltz and Meyer, *Z. anorg. Chem.*, 1928, **176**, 23). When, however, aluminium chloride reacts with ammonia, the stable volatile trichloroamminoaluminium (IX) is formed; this compound has now the "unimolecular" formula, since the aluminium atom has acquired five electrons and the bridged formulation is thus no longer possible; gallium trichloride behaves similarly (Klemm, Clausen, and Jacobi, *ibid.*, 1931, **200**, 343, 367; Klemm, Tilk, and Jacobi, *ibid.*, 1932, **207**, 187). The fact that aluminium chloride shows a molecular weight corresponding to $AlCl_3$ when dissolved particularly in co-ordinating solvents such as pyridine and ether may be due to simple dissociation, but is more probably due to the formation of soluble compounds similar to (IX) by linkage with solvent molecules.

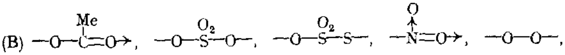
In all the bridged compounds discussed above, the nature of the bridging group has allowed (i) the simultaneous operation of a covalent and a co-ordinate link from this group, (ii) the formation of a 4-membered ring. Consideration of the chief groups known to bridge metallic atoms shows that many such groups bridge, however, by the operation of two covalent links: such groups occur more frequently in the 6-co-ordination salts, such as octammino-μ-imino-μ-sulphatodicobaltic chloride (X). Moreover, the nature of many bridging groups necessarily entails (if more than one group is present in the molecule) a bridged ring containing more than four atoms. Thus the bridging groups in (A) can all


(X.)


(XI.)

give 4-membered rings when two such groups bridge two metallic atoms, the type of linkages involved being indicated. The groups in (B) necessarily give rings with more than four atoms under similar conditions. The groups noted under (B) are the acetate group, which by resonance gives a symmetrical linkage; the sulphate and thiosulphate groups; the nitro-group, in which one of the oxygen atoms must co-ordinate to the metal,





since the nitrogen atom has no unshared pair of electrons available; the peroxide group, which gives a linkage of great stability, but may belong to the (A) group and have the

* It is of interest to note that formulæ precisely similar to (I) and (III) were suggested in 1909 by Werner (*op. cit.*, p. 52) for the compound $[PCl_3,PtCl_2]_2$.

structure $>O\rightarrow O$. In the palladium compounds described above, it is clear that 6-membered rings can be formed, since dinitrobis(tributylphosphine)-μ-dinitrodipalladium (XI) has been prepared (Mann and Purdie, *loc. cit.*). The *dinitrite-dichloride* derivative of trimethylarsine, $[Me_3As,Pd(NO_2)Cl]_2$, has therefore been prepared and is under investigation. This compound was obtained by the action of ammonium palladochloride on *dinitrobis(trimethylarsine)palladium*, $[(Me_3As)_2Pd(NO_2)_2]$, and it is probable therefore that in this compound the nitro-groups (and not the chlorine radicals) bridge the palladium atoms, with the production of a 6-membered ring.

Since the unsymmetrical and the *cis*-symmetrical forms (I and II) of the tetrachloride and tetrabromide compounds have not been detected in the solid state, we have, in collaboration with Dr. D. Purdie, investigated the phosphine and arsine derivatives of certain other metallic halides, particularly those of the mercuric halides. Preliminary experiments show that such isomerism does apparently occur in the crystalline state in such compounds. Thus di-iodobis(tri-*n*-propylphosphine)-μ-di-iododimercury, $[Pr^a_3P,HgI_2]_2$, has been isolated in two forms of correct molecular weight: one white and of m. p. 114° and the second yellow and convertible into the white form on heating. The apparent isomerism of these mercury derivatives is now being investigated in detail.

## EXPERIMENTAL.

### *Chemical Data.*

*Dichlorobis(trimethylarsine)palladium*, $[(Me_3As)_2PdCl_2]$.—The preparation of this compound from which almost all the subsequent compounds are derived, is considerably improved by the following method, which is speedy and avoids the troublesome isolation of trimethylarsine. A Grignard reagent was prepared by the action of methyl iodide (34 c.c., 78 g.) dissolved in ether (50 c.c.) upon magnesium (13 g., 4·5 atoms per 1 mol. $AsCl_3$) covered with ether (150 c.c.) in a flask fitted with a reflux condenser, mechanical stirrer, and a gas inlet tube; hydrogen was passed into the flask, and directly the reaction started, the mixture was cooled in ice-water to allow rapid addition of the methyl iodide without undue boiling of the ether. The mixture was then vigorously stirred, and the stirring and ice-cooling (in the atmosphere of hydrogen) continued until the final preparation of the arsine was complete. A solution of arsenic trichloride (10 c.c., 22 g.) in ether (50 c.c.) was next added, and when the reaction was complete hydrolysis was performed by the addition of ammonium chloride (50 g.) dissolved in cold freshly-boiled water (250 c.c.). The condenser was then replaced by a syphon-shaped tube, through which the solution was transferred by the pressure of hydrogen into a separating-funnel. The ethereal layer was separated, filtered if necessary, and at once shaken vigorously with increasing quantities of an aqueous solution of ammonium palladochloride. When about 16 g. of the latter had been added, a copious separation of the bright yellow dichloro-compound occurred; an excess of palladochloride must be avoided, otherwise the dichloro-compound becomes contaminated with the reddish-brown bridged tetrachloro-compound. (It is advisable, therefore, to withhold a few c.c. of the ethereal solution, which can then if necessary be added to the final product to decompose any brown tetrachloro-compound and thus restore the yellow colour of the dichloro-compound.) The dichloro-compound should be collected without delay, washed with water and dried, and can be used without further purification for the following preparations. Yield, *ca.* 21 g.

*Dibromobis(trimethylarsine)palladium.*—Solutions of the above dichloro-compound (5 g.) in boiling alcohol (200 c.c.) and of ammonium bromide (7 g., 6 mols.) in water (15 c.c.) were mixed, and boiled for 1 hour, the colour of the mixture changing rapidly to orange. On cooling, the *dibromo*-compound separated as orange needles, which, after recrystallisation from alcohol, had m. p. 229° (Found: C, 14·3; H, 3·5. $C_6H_{18}Br_2As_2Pd$ requires C, 14·2; H, 3·6%). The compound was also prepared by the action of trimethylarsine (2 mols.) upon an aqueous solution of ammonium palladobromide.

*Dichlorobis(trimethylarsine)-μ-dichlorodipalladium* (III).—The preparation of this compound, and its purification by recrystallisation from alcohol, have already been described (Mann and Purdie, *loc. cit.*). It can also be recrystallised from dioxan, acetic acid, and ethylene dichloride. Prolonged boiling with dioxan causes reduction, with separation of palladium. Hence, for recrystallisation sufficient dioxan must be taken to give a clear solution rapidly on boiling; the solution can then be allowed to cool spontaneously, since reduction does not occur

below the b. p. of dioxan. The well-formed crystals so obtained contain small quantities of dioxan, which is slowly lost in a vacuum without change of the crystal form. For instance, three different samples, after being in a vacuum for 24 hours, gave (i) C, 13·2; H, 2·9; (ii) C, 13·9; H, 3·2; (iii) Pd, 35·3 (Calc. for $C_6H_{18}Cl_4As_2Pd_2$: C, 12·1; H, 3·05; Pd, 35·85%). Rapid crystallisation from dioxan gave minute needles which readily lost all traces of the solvent in a vacuum and thus were soon obtained analytically pure.

*Dibromobis(trimethylarsine)-μ-dibromodipalladium.*—Hot solutions of dibromobis(trimethylarsine)palladium (2 g.) in alcohol (150 c.c.) and of ammonium palladobromide (1·8 g., 1 mol.) in water (15 c.c.) were mixed, and boiled under reflux for 30 minutes. The solution when filtered and cooled deposited the above *tetrabromide* in fine reddish-brown needles; after recrystallisation from alcohol, these decomposed at 258—260° with previous darkening but without melting (Found: C, 9·5; H, 2·5; Pd, 27·3. $C_6H_{18}Br_4As_2Pd_2$ requires C, 9·3; H, 2·3; Pd, 27·6%). Larger needles were obtained from dioxan, but these (like those of the above tetrachloride) contained traces of dioxan which were slowly lost in a vacuum: three different samples after 24 hours in a vacuum gave (i) C, 10·8; H, 2·3; (ii) C, 12·2; H, 2·9; (iii) Pd, 26·4.

*Dichlorobis(trimethylarsine)-μ-dibromodipalladium* (V).—This was prepared as the above tetrabromide, but from dibromobis(trimethylarsine)palladium (2 g.) and ammonium palladochloride (1·1 g., 1 mol.). The alcoholic solution on slow cooling deposited tetragonal needles of the *dichloride-dibromide*: these when recrystallised from alcohol, darkened on heating at 230° and by 248° had decomposed with the formation of a palladium mirror (Found: C, 10·5; H, 2·5; Pd, 31·0. $C_6H_{18}Cl_2Br_2As_2Pd_2$ requires C, 10·5; H, 2·6; Pd, 31·2%). The mother-liquor on long standing deposited compact monoclinic crystals (IV and V); these were collected, but were contaminated by a small proportion of the rhombic needles which started to separate during the filtration (Found, for the mixture: C, 10·5; H, 2·6%).

*Dithiocyanatobis(trimethylarsine)palladium.*—The finely-powdered dichloro-compound was added to excess of a cold concentrated aqueous solution of potassium thiocyanate. The mixture on shaking became at first brown, and later gave a copious precipitate of the yellow dithiocyanate. After 2 hours' shaking, the product was collected, washed with water, and twice recrystallised from alcohol; the *dithiocyanate* was thus obtained in deep yellow crystals, m. p. 124° (Found: C, 20·7; H, 3·9; N, 6·1. $C_8H_{18}N_2S_2As_2Pd$ requires C, 20·75; H, 3·9; N, 6·05%); when molten, it is deep red, and its hot concentrated alcoholic solution is also red, but deposits the yellow form unchanged on cooling.

*Dichlorobis(trimethylarsine)-μ-dithiocyanatodipalladium* (VI).—This was prepared by the usual method, hot alcoholic and aqueous solutions of the above dithiocyanate and of ammonium palladochloride (1 mol.) respectively being mixed and heated. The rapid change in colour indicated ready formation of the bridged complex, and after 5 minutes' heating, the solution was allowed to cool. The crystals which separated were dissolved in acetone, and the hot solution diluted with alcohol; the *dichloride-dithiocyanate* separated as minute dark orange crystals, m. p. 192—193° (decomp.) (Found: C, 15·4; H, 2·8; N, 4·5. $C_8H_{18}N_2Cl_2S_2As_2Pd_2$ requires C, 15·0; H, 2·8; N, 4·4%).

The *dibromide-dithiocyanate* was similarly prepared from ammonium palladobromide, and after recrystallisation from acetone was obtained as orange-red crystals, m. p. 189—190° (decomp.) (Found: C, 13·2; H, 2·45; N, 3·8. $C_8H_{18}N_2Br_2S_2As_2Pd_2$ requires C, 13·2; H, 2·7; N, 3·8%).

*Dinitrobis(trimethylarsine)palladium.*—The finely powdered dichloro-compound was shaken with excess of a cold concentrated aqueous solution of sodium nitrite for 2 hours, by which time the yellow dichloro-compound had been entirely replaced by the almost white *dinitro*-compound; this was collected, washed with water, and recrystallised from alcohol–acetone, being obtained as very pale lemon-coloured crystals, m. p. 234° (decomp.) (Found: N, 6·3; Pd, 24·0. $C_6H_{18}O_4N_2As_2Pd$ requires N, 6·4; Pd, 24·3%).

*Dichlorobis(trimethylarsine)-μ-dinitrodipalladium.*—A hot solution of ammonium palladochloride (1·3 g.) in water (4 c.c.) and alcohol (20 c.c.) was added to a boiling solution of the foregoing compound (2 g., 1 mol.) in alcohol (100 c.c.), and the mixture, the colour of which changed rapidly to reddish-orange, was at once allowed to cool spontaneously. After 24 hours, a fine, microcrystalline, buff-coloured deposit was separated, and the filtrate set aside for a further 48 hours. Fine, pale orange crystals of the *dinitro-dichloride* slowly developed: these, when collected, washed with water, and dried, had m. p. 186—188° (decomp. with preliminary softening) (Found: C, 11·8; H, 3·3; N, 4·4. $C_6H_{18}O_4N_2Cl_2As_2Pd_2$ requires C, 11·7; H, 2·9; N, 4·5%).

In the above preparation the mixed solution must not be boiled, otherwise the nitro-groups

are evicted with the formation of $[(Me_3As)_2PdCl_2]$. A similar experiment in which ammonium palladobromide was used, with 30 minutes' boiling, gave chiefly $[(Me_3As)_2PdBr_2]$.

The tetranitrite, $[(Me_3As)Pd(NO_2)_2]_2$, appears to be very unstable. When a suspension of the powdered tetrachloride in concentrated aqueous potassium nitrite was gently warmed for a few seconds, reaction occurred with splitting of the bridged linkage and formation of $[(Me_3As)_2Pd(NO_2)_2]$ and ammonium palladonitrite.

*Trimethylphosphine.*—This compound is so reactive that it cannot be prepared by the usual methods. We are indebted to Dr. D. Purdie for the following method of isolating the phosphine as the silver iodide derivative, $[Me_3P{\rightarrow}AsI]_4$ (Mann, Wells, and Purdie, J., 1937, 1828), from which the phosphine can be regenerated when required. An ethereal solution of methylmagnesium iodide was prepared from magnesium (24 g., 6 atoms per 1 mol. $PCl_3$), methyl iodide (60·5 c.c., 138 g.), and ether (300 c.c.) in a 3-necked flask with ground glass connexions for a reflux condenser, inlet-tube for hydrogen, and mechanical stirrer. The product was strongly cooled, and a solution of phosphorus trichloride (14 c.c., 22·5 g.) in ether (50 c.c.) slowly added with vigorous stirring. The flask was then kept at room temperature for 30 minutes, and the solution (without hydrolysis) distilled directly from an oil-bath, the temperature of which was finally taken to 200° until no further distillate was obtained. The stream of hydrogen was continued throughout the preparation until this distillation was complete. The ethereal distillate was then without delay shaken with a solution of silver iodide in aqueous potassium iodide solution. The white solid was filtered, washed, and well pressed in drying paper. This silver iodide derivative is too unstable to be recrystallised: when dry, it can be kept indefinitely in a sealed tube. To regenerate the trimethylphosphine, the silver derivative was heated gently in one arm of an inverted U-tube, the other arm being immersed in a freezing mixture. The silver derivative dissociated, and the pure phosphine collected in the cold arm; it was used at once, otherwise at room temperature the silver iodide reabsorbed it, becoming white again.

*Dichlorobis(trimethylphosphine)palladium.*—Prepared in the usual way, and recrystallised from alcohol, this was obtained as pale yellow crystals, m. p. 282° (decomp.) (Found: C, 21·7; H, 5·2. $C_6H_{18}Cl_2P_2Pd$ requires C, 21·8; H, 5·45%).

*Dichlorobis(trimethylphosphine)-μ-dichlorodipalladium.*—This compound was prepared in the usual way by the action of ammonium palladochloride upon the foregoing compound in alcoholic solution, from which it separated as beautiful, well-formed, red crystals, m. p. 285° (decomp.) with preliminary darkening and shrinking (Found: C, 14·0; H, 3·7; Pd, 42·0. $C_6H_{18}Cl_4P_2Pd_2$ requires C, 14·2; H, 3·55; Pd, 42·1%).

### *Crystallographic Data.*

In view of the voluminous nature of the observations and evidence obtained (in particular) in the complete analysis of the tetrabromide, only the essential points in this evidence are given below: the full detailed evidence will be published elsewhere.

*Dichlorobis(trimethylarsine)-μ-dichlorodipalladium* (III) *and Dibromobis(trimethylarsine)-μ-dibromodipalladium.*—The tetrachloride crystallises from alcohol and from dioxan as isomorphous tetragonal prisms {110} showing high negative birefringence and pleochroism, the light transmitted being pale yellow for vibrations along the needle axis and orange-red perpendicular to that axis. The crystals are not pyroelectric. The cell dimensions of the crystals from dioxan are about 1·5% greater than those of the crystals from alcohol: from dioxan, $a = 16{\cdot}25$; $c = 7{\cdot}31$ A.; from alcohol, $a = 16{\cdot}0$; $c = 7{\cdot}22$ A. Oscillation and Weissenberg photographs show that the space group is $I4$, $I\bar{4}$ or $I4/m$.

The tetrabromide crystallises from dioxan as tetragonal prisms isomorphous with those of the tetrachloride and with cell dimensions $a = 16{\cdot}6$; $c = 7{\cdot}48$ A. The approximate density was determined by flotation (2·5 g./c.c.): that calculated for 4 molecules of $[Me_3As,PdBr_2]_2$ per unit cell is 2·48 g./c.c. Crystals of the tetrabromide from alcohol, however, are not tetragonal, and on account of their poor quality they were not further examined. The spacing along the needle axis of these crystals from alcohol is 7·41 A., and it is clear that their structure is only a distortion of that of the tetragonal crystals from dioxan. From $X$-ray photographs of the three isomorphous tetragonal crystals (tetrachloride from alcohol and dioxan, and tetrabromide from dioxan) it is obvious that their structures differ only in detail.

The optical properties and cell dimensions suggested that this structure was built up of planar molecules lying in planes parallel to (001), and an $F^2$ projection on the $ac$ plane confirmed the planar nature of the molecules. Whichever of the three possible space-groups is chosen, the planar molecule must possess a diad axis of symmetry perpendicular to the plane

of the molecule. This implies that the molecules in the crystal must have the *trans*-symmetrical structure (III; or with Br for Cl). The space group $I4/m$ was finally adopted, in which the molecular symmetry is $2/m$. The plane of symmetry merely raises the symmetry of the $Me_3As$ group. The mutual orientation of the molecules in planes at $z = 0$ and $z = \frac{1}{2}$ was first found by trial and error methods, and finally determined (together with the configuration of the molecule itself) from a section at $z = 0$ of the three-dimensional electron-density distribution. The structure may therefore be represented as in Fig. 1. In the tetrabromide the molecules lie with their Pd–Pd axes inclined at 1·5° to the *a* axes. The configuration of the tetrabromide molecule was finally determined as that shown in Fig. 2.

A notable feature of the structure of the tetrachloride and tetrabromide is the existence of approximately cylindrical tunnels parallel to the *c* axis. The diameter of these tunnels is about that of the dioxan molecule if this molecule is assumed to be an oblate spheroid of effective radius 3·45 A. (Fig. 1). In the crystals of the tetrachloride from alcohol these tunnels are empty, but when the crystals are grown from dioxan they are filled—either partly or completely—by molecules of the solvent. Since the axis of the holes is a four-fold axis of symmetry, it is to be concluded that the dioxan molecules are rotating in the crystal.

If a configuration for the molecule of the tetrachloride analogous to that of the tetrabromide is assumed (allowing for the difference in size between Br and Cl), the high-order intensities may be used to determine the inclination of the molecule to the axes in the crystals from alcohol and from dioxan. Good agreement is obtained with the molecules inclined at 2° to the axes in the crystals from alcohol, and parallel to the axes in the crystals from dioxan. In all cases the positions of the carbon atoms were determined by considerations of packing. The agreement between calculated and observed structure factors for the tetrachloride and tetrabromide from dioxan is shown in the table for a number of reflexions. Intensities were estimated visually on Weissenberg photographs, the intensity scale being adjusted to make the values of $F'$, obs., and $F$, calc., comparable for low orders, where $F' = [I_{obs.} \sin 2\theta/(1 + \cos^2 2\theta)]^{\frac{1}{2}}$. The values of $F$, calc., are those for the following parameters:

| | | Tetrabromide. | | | | Tetrachloride. | | |
|---|---|---|---|---|---|---|---|---|
| | | *x*. | *y*. | *z*. | | *x*. | *y*. | *z*. |
| Pd | 8(*h*) | 0·608 | 0·003 | 0 | Pd | 0·604 | 0 | 0 |
| As | 8(*h*) | 0·715 | 0·109 | 0 | As | 0·716 | 0·106 | 0 |
| $Br^1$ | 8(*h*) | 0·497 | 0·101 | 0 | $Cl^1$ | 0·500 | 0·097 | 0 |
| $Br^2$ | 8(*h*) | 0·717 | – 0·094 | 0 | $Cl^2$ | 0·708 | – 0·096 | 0 |
| C | 16(*i*) | 0·783 | 0·100 | 0·212 | C | 0·785 | 0·100 | 0·217 |
| | 8(*h*) | 0·669 | 0·219 | 0 | | 0·669 | 0·218 | 0 |

$Br^1$ and $Cl^1$ represent halogen atoms linked each to two palladium atoms, $Br^2$ and $Cl^2$ those linked to only one palladium atom.

(Space-group nomenclature: International Tables.)

Tetrachloride from dioxan.

| *hkl*. | $F'$, obs. | $F$, calc. | *hkl*. | $F'$, obs. | $F$, calc. |
|---|---|---|---|---|---|
| 200 | 14 | +13 | 501 | 5 | – 9 |
| 400 | <4 | – 1 | 701 | 15 | +19 |
| 600 | 8 | – 7 | 901 | <7 | + 3 |
| 800 | 22 | +27 | *11*01 | 9 | +16 |
| *10*00 | 56 | +52 | | | |
| | | | 002 | 67 | +73 |
| 101 | 11 | +13 | 004 | 57 | +64 |
| 301 | 20 | +22 | 006 | 28 | +48 |

Tetrabromide from dioxan.

| *hkl*. | $F'$, obs. | $F$, calc. | *hkl*. | $F'$, obs. | $F$, calc. |
|---|---|---|---|---|---|
| 200 | 26 | +18 | 110 | 53 | –57 |
| 400 | <4 | 0 | 220 | 3 | + 2 |
| 600 | 16 | –16 | 330 | 17 | +16 |
| 800 | 33 | +44 | 440 | 63 | –73 |
| *10*00 | 59 | +67 | 550 | 73 | +80 |
| | | | 660 | 26 | –23 |
| 101 | 11 | +16 | 770 | <6 | + 2 |
| 301 | 15 | +15 | 880 | 15 | +19 |
| 501 | 33 | –33 | 990 | 41 | –50 |
| 701 | 18 | +12 | *1010*0 | 38 | +46 |
| 901 | <7 | – 2 | | | |
| *11*01 | 19 | +25 | | | |

*Dichlorobis(trimethylarsine)-μ-dibromodipalladium* (V).—Three different crystalline forms of this compound were examined.

(i) *The first main crop of needles from alcohol.* These were very similar in appearance to the tetragonal needles of the tetrachloride and tetrabromide, and showed the same pleochroism. The crystals were very imperfect and easily split along the needle axis. They are apparently monoclinic, and the fact that the spacing along the needle axis is 7·34 A., together with the pleochroism, suggests that their structure is, like that of the tetrabromide crystals from alcohol, closely related to the tetragonal structure already described.

(ii) *Monoclinic crystals which separated from the alcoholic mother-liquor on standing.* Com-

pact monoclinic crystals, with the forms {001} and {110}, sometimes elongated along the *c* axis. Cell dimensions are $a = 12{\cdot}1$, $b = 10{\cdot}6$, $c = 6{\cdot}83$ A., $\beta = 72°$. For a density of 2·70 the unit cell contains 2 molecules of $[Me_3As,PdClBr]_2$. The halvings were 0*k*0 for *k* odd and *h*0*l* for *h* odd; the space-group is therefore $P\,2_1/a$. Since there are only 2 molecules of the bridged complex in the unit cell, these molecules must be centro-symmetrical. Hence the configuration of the molecule must be (IV) or (V).

(iii) *Rhombic needles which separated with the monoclinic crystals* (ii) *above.* These needles {110} have the cell dimensions: $a = 23{\cdot}4$, $b = 12{\cdot}7$, $c = 11{\cdot}4$. For a density of 2·67, the cell contains 8 molecules of $[Me_3As,PdClBr]_2$. The space group is *P ccn*: in this space group the 8 molecules could occupy two 4-fold positions with point symmetry $\bar{1}$, two sets of 4-fold positions with symmetry 2, or an 8-fold position without symmetry. It is therefore impossible to draw any conclusions with regard to the symmetry of the molecules in these crystals.

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The University Chemical and Crystallographic Laboratories,
Cambridge. [*Received, March 21st*, 1938.]

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## 130. *Analogues of Ascorbic Acid containing Six-membered Rings.*

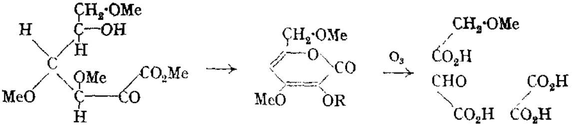
By W. N. Haworth, E. L. Hirst, and J. K. N. Jones.

It is shown that, by the action of sodium methoxide, or by continued heating under diminished pressure, esters (I) of methylated 2-ketogluconic acids having a free hydroxyl group at $C_5$ are converted into derivatives (II) of α-pyrone. These may be regarded as analogues of ascorbic acid containing six-membered rings and they have properties similar to those of 3-methyl ascorbic acid and absorption spectra generally resembling those displayed by members of the ascorbic acid series but with the heads of the bands situated at somewhat longer wave-lengths. The structure of the new substances is proved and a series of substituted α-pyrones has been prepared for comparison. It has now become possible to identify as the α-pyrone derivative (II, R = H) the substance, $C_8H_{10}O_5$, m. p. 89°, which is found consistently as one of the oxidation products of tetramethyl fructofuranose.

Several analogues of ascorbic acid possessing the normal five-membered ring structure have been prepared and for comparison with these we wished to obtain substances similar in constitution except as regards the nature of the lactone ring. Preliminary attempts to synthesise such compounds by the action of hydrogen cyanide on the osones of 3 : 5 : 6-trimethyl glucose and 3-methyl glucose were abandoned, in the former case because the osone was not readily obtainable from the osazone, and in the latter because of the unexpected behaviour of the addition product, which did not rearrange to form a substance analogous to ascorbic acid (compare Haworth, Hirst, Jones, and Smith, J., 1934, 1192).

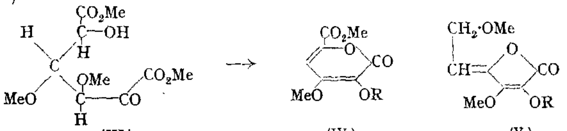
We then turned our attention to the action of sodium methoxide on the methyl esters of 3 : 4 : 6-trimethyl 2-ketogluconic acid (I). By analogy with the well-known reaction for the synthesis of ascorbic acid, this would be expected to give a methylated analogue of *d*-arabo-ascorbic acid containing a δ-lactone ring. It was found, however, that the reaction proceeds beyond this stage, with elimination of methyl alcohol between $C_4$ and $C_5$ and formation of the *α-pyrone* derivative (II, R = H). A similar procedure, starting from the ester of the dibasic acid (III), gives the corresponding *α-pyrone-6-carboxylate* (IV, R = H). The reactions of these towards diazomethane [which produces the corresponding *3-methyl* derivatives (II, R = Me) and (IV, R = Me)], acid iodine, Fehling's solution, sodium hypoiodite, and alkaline permanganate are closely similar to those previously observed with 3-methyl ascorbic acid (Haworth, Hirst, and Smith, J., 1934, 1556) except

that, as would be expected, some iodoform is produced by the action of sodium hypoiodite on (II, R = H). All the new substances are optically inactive.



(I.) (II.)

The presence of the α-pyrone ring structure in (II) and (IV) is supported by the following observations. The close similarities in mode of preparation, properties, and absorption spectra of (II, R = H) and (IV, R = H) point definitely to identity of ring structure, and since the latter has a terminal carboxy-group the presence of a 1 : 6-lactone ring is automatically ruled out. The formation of the five-membered ring (V) from (I) would involve the elimination of dimethyl ether between the CO·OMe group and the OMe at $C_4$, a reaction which is highly improbable when the much more facile elimination of methyl alcohol at $C_5$ can readily take place. Moreover, experiment showed that glyoxylic acid, recognised by its characteristic colour reaction, was one of the products of ozonisation of (II, R = H), and this can be formed on ozonisation only if the ring structure is the six-membered one shown in (IV). It cannot arise from (V). For these reasons we assign to all the above-mentioned substances the α-pyrone structure, and further support for this view was found in a comparison of the absorption spectra of the various substances with those of some typical hydroxylated α-pyrones and their methyl ethers, which were prepared specially for this purpose. Some of these, *e.g.*, (VII, R = Me), have not hitherto been described and in the course of the work we came across the open-chain *compound* (VI, R = H), which on treatment with diazomethane passes smoothly into the *methylated* derivative (VI, R = Me). The structure follows from the mode of preparation (see experimental section).



(III.) (IV.) (V.)

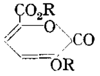
The absorption spectra of the α-pyrones resemble, in general, that of ascorbic acid in showing an intense band in the ultra-violet region, but owing to the increased conjugation the head of the band is situated closer to the visible spectrum. There are indications in some cases of the presence of a weaker band further in the ultra-violet, and coumalic acid (VIII), which is differently constituted, displays a markedly different absorption spectrum. Substance (VII, R = H), judging from the intensity of the band at λ 3200 A., exists in solution largely in the keto-form, this observation being in agreement with its behaviour towards ferric chloride. On methylation the enolic form is produced and the band is seen at its full intensity. Methyl 3 : 4 : 6-trimethyl 2-ketogluconate, which appears to exist mainly in the lactol form, does not display selective absorption in the ultra-violet.

Two other points of special interest emerge from the work described. The substance (II, R = H) is obtainable also by the slow distillation of (I) under diminished pressure, this fact being another argument in favour of the six-membered ring structure for (II). The reaction resembles that observed by Votoček and Malachata (*Coll. Czech. Chem. Comm.*, 1936, 8, 66), who obtained α-pyrone derivatives by the distillation of lactones. Reference to the early work on the structure of sucrose shows that on oxidation of tetramethyl γ-fructose by nitric acid, a crystalline substance, $C_8H_{10}O_5$, m. p. 89°, was consistently obtained in small yield (Haworth and Linnell, J., 1923, 123, 294; Haworth and Hirst, J.,

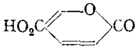
1926, 1858). The structural relationships of this material, which at the time was considered to be a furan derivative, have hitherto been uncertain, but it now appears that it is identical with the α-pyrone (II, R = H). The derivation of the substance from tetramethyl fructofuranose is now clear and a simple explanation becomes possible of the difficulties of interpretation commented upon in the earlier papers.

$$\begin{array}{l} \text{CH:C(OR)}\cdot\text{CO}_2\text{R} \\ \text{CH:C(OR)}\cdot\text{CO}_2\text{R} \end{array}$$

(VI.)



(VII.)



(VIII.)

The other point is that the *substance* (VII, R = Me), m. p. 215°, appears to be identical with a substance, $C_8H_8O_5$, m. p. 215°, encountered incidentally by Schmidt, Dippold, and Zeiser (*Ber.*, 1937, **70**, 2413) in the course of their work on the action of diazomethane on saccharic acid. These workers were unable to assign a definite structure to the substance, but a comparison of its properties with those of (VII, R = Me) indicates that in all probability it had the α-pyrone structure shown in (VII), a result which can be readily interpreted in the light of the other observations made by these authors.

## EXPERIMENTAL.

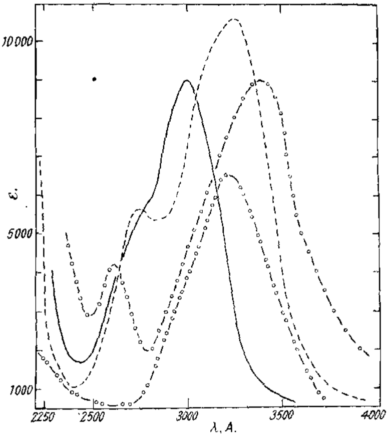
*Addition of Hydrogen Cyanide to 3-Methyl Glucosone.*—3-Methyl glucosazone (J., 1929, 1935) (50 g.) was stirred for 30 minutes at 20° with fuming hydrochloric acid (200 c.c.). The mixture was cooled (ice–salt), and the phenylhydrazine hydrochloride separated by filtration. The solution containing 3-methyl glucosone was neutralised with lead carbonate and filtered, lead acetate (50 g.) added, and sodium hydroxide stirred in until the solution was slightly alkaline. The lead hydroxide–osone complex was separated on the centrifuge and the osone was regenerated by addition of the requisite quantity of dilute sulphuric acid. The aqueous solution of 3-methyl glucosone so obtained gave the osazone rapidly on addition of phenylhydrazine at 40°. The osone did not reduce Fehling's solution in the cold, but did so readily on warming. Oxygen was displaced from the solution containing the osone by passing a rapid stream of nitrogen, and an excess of solid potassium cyanide and a little calcium chloride solution were then added. After 40 minutes the solution contained no material which reacted with iodine in acid solution. The product was isolated in the way described for the synthesis of ascorbic acid (Haworth, Hirst, Jones, and Smith, J., 1934, 1192) and was obtained as a brown syrup, which was acidic, reduced hot Fehling's solution, did not give 3-methyl glucosazone on treatment with phenylhydrazine, and did not react with iodine in acid solution. The methyl ester of this product was prepared and treated with sodium methoxide (compare Maurer and Schiedt, *Ber.*, 1933, **66**, 1054), but no material resembling ascorbic acid in its chemical properties was obtainable. In other experiments the addition of hydrogen cyanide was carried out in the presence of methyl chloroformate (compare Haworth and Peat, J., 1929, 354), but no substance analogous to ascorbic acid was encountered when the final product was isolated.

*Preparation of Methyl 3-Hydroxy-4-methoxy-α-pyrone-6-carboxylate from 1 : 3 : 4 : 6-Tetramethyl Fructose.*—1 : 3 : 4 : 6-Tetramethyl fructose (Menzies, J., 1922, 2238) was oxidised with nitric acid (*d* 1·42) (Haworth, Hirst, and Nicholson, J., 1927, 1520). The product contained monobasic and dibasic acids and was isolated as a syrup composed of the corresponding methyl esters. This crude syrup (without attempted purification by distillation: see below) (20 g.) was heated for 1 hour at 70° with methyl-alcoholic sodium methoxide (90 c.c., 1·4N). Yellow crystals separated, which were filtered off (filtrate A), washed rapidly with methyl alcohol, and dried in a vacuum. This sodium derivative was digested with methyl-alcoholic hydrogen chloride, giving in good yield *methyl 3-hydroxy-4-methoxy-α-pyrone-6-carboxylate* (IV, R = H) as colourless crystals, m. p. 207° after recrystallisation from methyl alcohol, sparingly soluble in the cold in water, methyl alcohol, acetone, and ether, readily in hot water and hot methyl alcohol (Found: C, 48·3; H, 4·2; OMe, 30·4. $C_8H_8O_6$ requires C, 48·0; H, 4·0; OMe, 31·0%). It was acid to litmus and Congo-paper, gave an orange colour in the presence of warm alkali, reduced hot Fehling's solution, and gave a greyish-blue colour with alcoholic ferric chloride. On treatment with alkaline potassium permanganate it gave oxalic acid (isolated as the calcium salt) in a yield of 80% of the theoretical calculated for formation of three molecules of oxalic

cid. Oxalic acid was formed also on ozonisation in glacial acetic acid. For the absorption spectrum, see Fig. 1.

*Methyl* 3 : 4-*Dimethoxy-α-pyrone*-6-*carboxylate* (IV, R = Me).—Substance (IV, R = H) was issolved in dry methyl alcohol, and an excess of ethereal diazomethane added. After 12 hours t 0° the solution was concentrated under diminished pressure at 30°, giving a crystalline mass which on recrystallisation from methyl alcohol gave *methyl* 3 : 4-*dimethoxy-α-pyrone*-6-*carboxylate* n long needles, m. p. 93°, sparingly soluble in water and in ether; readily soluble in methyl alcohol and in acetone (Found: C, 50·6; H, 4·7; OMe, 42·1. $C_9H_{10}O_6$ requires C, 50·5; H, 4·7; OMe, 43·5%). It was neutral to Congo-red, gave no colour with alcoholic ferric chloride, was non-reducing to boiling Fehling's solution, and formed a yellow solution in hot alkali. For absorption spectrum, see Fig. 1.

FIG. 1.




— — — — 3-*Hydroxy*-4-*methoxy*-6-*hydroxymethyl-α-pyrone in methyl alcohol.*
———— 3 : 4-*Dimethoxy*-6-*hydroxymethyl-α-pyrone in water.*
—o—o— *Methyl* 3-*hydroxy*-4-*methoxy-α-pyrone*-6-*carboxylate in methyl alcohol.*
—oo—oo— *Methyl* 3 : 4-*dimethoxy-α-pyrone*-6-*carboxylate in methyl alcohol.*
(*Concentration in each instance* ca. 3 *mg.*/100 *c.c.*)

3-*Hydroxy*-4-*methoxy*-6-*methoxymethyl-α-pyrone* (II, R = H) *from* 1 : 3 : 4 : 6-*Tetramethyl Fructose*.—The filtrate (A) (p. 712) was rendered slightly acid with methyl-alcoholic hydrogen chloride, the sodium chloride removed, and the filtrate concentrated under diminished pressure. After some time a crystalline mass was deposited. This was extracted with ether, which dissolved substance (II, R = H), leaving a residue containing sodium chloride and a further quantity of substance (IV, R = H), m. p. 207° (see p. 712). The ethereal solution on evaporation gave 3-*hydroxy*-4-*methoxy*-6-*methoxymethyl-α-pyrone* (II, R = H), m. p. 88° after recrystallisation from methyl alcohol (Found: C, 51·9; H, 5·4; OMe, 33·9. $C_8H_{10}O_5$ requires C, 51·7; H, 5·3; OMe, 33·3%). For absorption spectrum, see Fig. 1. The pyrone was soluble in water and in the usual organic solvents except light petroleum. It was acid to litmus, reduced Fehling's solution, and gave a yellow colour with alkali, a red colour with a trace of alcoholic ferric chloride and a deep blue colour with larger quantities. With iodine in acidified aqueous solution it reacted slowly, using up 2 atomic proportions (0·100 g. required 11·4 c.c. of N/10-iodine. Calc., 11·1 c.c.). Sodium hypoiodite in slightly alkaline solution reacted with (II, R = H), giving iodoform (36·6 mg. gave 10·6 mg. of iodoform and required 14·1 c.c. of N/10-iodine; the conversion into oxalic acid, methoxyacetic acid, and iodoform is incomplete, since this requires 19·5 c.c. of

N/10-iodine and would liberate 77 mg. of iodoform). Ozonisation of the compound (1·76 g.) in purified glacial acetic acid (40 c.c.) gave oxalic acid (0·465 g.; isolated as the calcium salt; calc., 0·837 g.) and the filtrate after removal of the calcium oxalate then gave the characteristic colour reactions for glyoxylic acid (purple colour with casein and hydrochloric acid). In another experiment, pure carbon tetrachloride was used as solvent, and the same results obtained after ozonisation. The pyrone (II, R = H) reduced neutral alkaline potassium permanganate solution [20 mg. required 31·24 c.c. of N/25-neutral potassium permanganate at 0°; calc. for oxidation to oxalic acid (2 mols.) and methoxyacetic acid (1 mol.), 23·4 c.c. The yield of oxalic acid, isolated as the calcium salt, was 75% of the theoretical].

The above substance (II, R = H) could also be obtained by slow distillation at 200°/12 mm. of the mixed methyl esters (16·5 g.) prepared by the oxidation of 1 : 3 : 4 : 6-tetramethyl fructose (for method, see above). As distillation proceeded, the refractive index of the distillate rose from $n_D^{20°}$ 1·4385 to 1·5100. Three fractions were collected and the distillate gave a more intense blue colour with alcoholic ferric chloride as the b. p. and $n_D$ increased: (*a*) b. p. 180°/12 mm., $n_D^{20°}$ 1·4500 (12 g.); (*b*) b. p. 190°/12 mm., $n_D^{20°}$ 1·4675 (6·3 g.); (*c*) b. p. 190°/12 mm., $n_D^{20°}$ 1·4812 (1·5 g.). Fractions (*a*) and (*b*) were united and redistilled, giving a further fraction similar in properties to fraction (*c*). On nucleation with substance (II, R = H), both fractions crystallised and on trituration with ether gave the crystalline solid, m. p. 88° (after recrystallisation from ether). A mixed m. p. with a specimen prepared by the first method showed no depression.

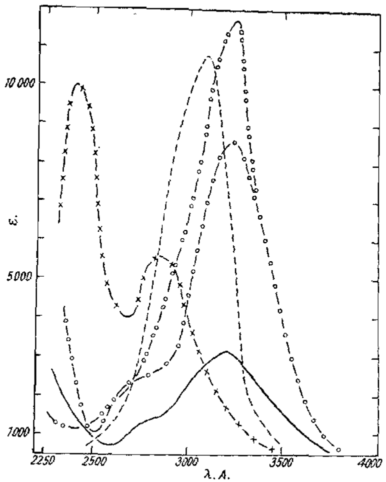
3 : 4-*Dimethoxy-6-methoxymethyl-α-pyrone* (II, R = Me).—Substance (II, R = H) (0·5 g.) was dissolved in dry methyl alcohol, and an excess of ethereal diazomethane added at 0°. After 20 hours at − 15°, the solution no longer gave a colour with alcoholic ferric chloride. The solvent was removed at 40°/12 mm., leaving a yellow syrup, $n_D^{20°}$ 1·5270 (Found: OMe, 46·0. $C_9H_{12}O_5$ requires OMe, 46·5%). The crude syrup was distilled at 135°/0·02 mm. (bath temp.), giving 3 : 4-*dimethoxy-6-methoxymethyl-α-pyrone* (II, R = Me) (0·46 g.), $n_D^{20°}$ 1·5280, $[\alpha]_D^{20°}$ ± 0° in water (*c* = 1·2), as an orange syrup, soluble in all the usual solvents except light petroleum. In aqueous solution it reacted neutral to litmus and gave no colour with alcoholic ferric chloride (Found: C, 53·9; H, 6·4; OMe, 46·4. $C_9H_{12}O_5$ requires C, 54·0; H, 6·0; OMe, 46·5%). No free hydroxyl groups were present, since the substance was recovered unchanged after treatment with Purdie's reagents. The syrup (II, R = Me) reduced cold acid potassium permanganate solution (16·4 mg. required 22·22 c.c. of N/25-$KMnO_4$. Calc., 20·4 c.c. for oxidation to 2 mols. of oxalic acid and 1 mol. of methoxyacetic acid). For absorption spectrum, see Fig. 1.

*αα'-Diketoadipic Acid.*—Ethyl oxalate and ethyl succinate were condensed in ethereal solution by the method of Blaise and Gault (*Comp. rend.*, 1909, **148**, 177), sodium ethoxide at 15° being used. After 48 hours, the mixture was poured into water and acidified with hydrochloric acid and the oil which separated was extracted with ether. The syrup so obtained was dissolved in cold concentrated hydrochloric acid and left for 24 hours. It was then diluted with water and heated at 90° until evolution of carbon dioxide had ceased. Hydrochloric acid was removed by distillation with frequent additions of water. The concentrated solution finally obtained deposited oxalic and succinic acids, which were filtered off. On further concentration yellow crystals were deposited, which were triturated with ether. By continued extraction with ether the yellow material was separated into two portions: (*a*) (ether-soluble) 3-hydroxy-α-pyrone-6-carboxylic acid, (VII, R = H), m. p. 90°, solidifying at higher temps. (loss of carbon dioxide) and decomposing at 207° (Found: *M*, 158. Calc., 156), identical with the substance described by Blaise and Gault (for absorption spectrum, see Fig. 2); (*b*) (ether-insoluble) *αα'-diketoadipic acid* (VI, R = H), m. p. 227° (Found: C, 41·5; H, 3·26; *M*, 176. $C_6H_6O_6$ requires C, 41·4; H, 3·4%; *M*, 174). The latter was a yellow solid almost insoluble in water and in most organic solvents, but slightly soluble in chloroform. It gave a fleeting purple colour with alcoholic ferric chloride, reduced warm Fehling's solution, and was slowly oxidised by iodine in aqueous acid solution. In an excess of alkali it formed an orange-coloured solution. In aqueous solution the material showed an acidic reaction and gave a green colour with ferric chloride. For absorption spectrum, see Fig. 2. Titration of the material, dissolved in methyl alcohol, with ethereal diazomethane at − 10° gave the *tetramethyl* derivative (VI, R = Me), isolated on concentration of the solution at 30°/15 mm. as long needles, m. p. 116° (Found: OMe, 52·6. $C_{10}H_{14}O_6$ requires OMe 53·8%). For absorption spectrum, see Fig. 2.

*Methyl 3-Methoxy-α-pyrone-6-carboxylate* (VII, R = Me).—3-Hydroxy-α-pyrone-6-carboxylic acid (VII, R = H) reacted with diazomethane in methyl-alcoholic solution to give *methyl 3-methoxy-α-pyrone-6-carboxylate*, m. p. 215° (sublimes) (after recrystallisation from methyl

alcohol). This derivative was also prepared from (VII, R = H) by methylation with Purdie's reagent. It was isolated as a white crystalline solid, sparingly soluble in the cold in the usual organic solvents, soluble in hot methyl alcohol and hot water. It gave no colour with ferric

FIG. 2.




——— *3-Hydroxy-α-pyrone-6-carboxylic acid in water.*
— — — *Methyl 3-methoxy-α-pyrone-6-carboxylate in methyl alcohol.*
—o—o— *αα'-Diketoadipic acid in methyl alcohol.*
—oo—oo— *Methyl O-dimethyl-αα'-diketoadipate (enolic form) in methyl alcohol.*
—x—x— *Coumalic acid in water.*
(*Concentrations* ca. 3 *mg.*/100 *c.c.*)

chloride solution, was neutral in reaction, and did not reduce Fehling's solution (Found: C, 51·9; H, 4·4; OMe, 32·9. $C_8H_8O_5$ requires C, 52·2; H, 4·4; OMe, 33·6%). For absorption spectrum, see Fig. 2. For comparison the absorption spectrum of coumalic acid (VIII) is shown in Fig. 2.

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# 131. *The Determination of the Vapour Densities of Indigo and Other Organic Compounds by Means of a Spoon Gauge.*

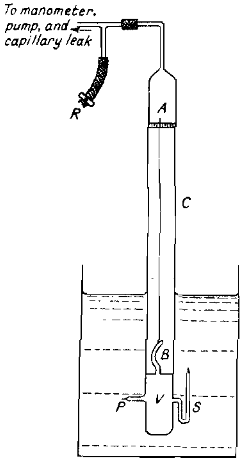
By C. E. DENT and R. P. LINSTEAD.

The application of the spoon gauge to the determination of the molecular weights of volatile organic compounds is described. The molecular weights of indigo, phthalimide, and of the polymeride of phthalonitrile are recorded.

SOME years ago we attempted the direct measurement of the vapour densities of stable organic compounds at high temperatures in connexion with an investigation of the molecular weights of various phthalocyanines. For this purpose an apparatus embodying a spoon gauge was utilised, such as has been used for certain inorganic substances (see, *e.g.*,

Jackson, J., 1910, **99**, 1066; Smits, J., 1924, **125**, 2554) but not previously, as far as we are aware, for organic compounds. In this apparatus a measurement is made of the pressure exerted by a known weight of the substance under investigation when completely volatilised and occupying a known volume. The advantages of the method are (I) that it requires only small amounts of material (10—50 mg.), and (2) that it can be used at temperatures (200—400°) which may be inconvenient for the usual vapour-density methods. Hence it is particularly useful for more complex molecules. Its application is, of course, limited to thermally stable substances.

The molecular weight of indigo at 430° was found to be 257 ± 9, in agreement with the monomeric formula (*M*, 262). The vapour of phthalimide was monomeric over the range 295—340°. The polymeride of phthalonitrile of m. p. 296° (Linstead and Lowe, J, 1934, 1025) was found to be trimeric, from measurements at 420—430°. This suggests strongly that it is tricyanocyaphenine. This very stable substance may be crystallised from hot concentrated nitric acid without decomposition, but on long standing with this reagent it undergoes fission to phthalimide.




An attempt to determine the vapour density of copper phthalocyanine failed, as the spring began to bend under its own weight at about 500°. After 30 minutes at this temperature the copper phthalocyanine was recovered unchanged. No pressure was developed, showing that no decomposition or sublimation occurs at this temperature (compare Dent and Linstead, J., 1934, 1027).

## Experimental.

The apparatus is shown in the figure. A convenient weight of the substance was weighed into the side arm *S*, which was then sealed. The apparatus, made of Pyrex glass, was then evacuated, the side tube *P* being open and connected to *R* by pressure tubing. During this process as much as possible of the lower chamber *V* was heated, care being taken to avoid volatilising the substance in *S*. The tubing between *P* and *R* was then closed with a pinchcock, and *P* was sealed off. The apparatus was then immersed in an insulated and mechanically-stirred bath of fused nitrates to the level indicated, and the pointer *A* on the glass spring *B* was kept at zero by altering the pressure in the upper chamber *C*; this was connected to a manometer, to a large reservoir, and to a three-way tap, joined to a pump and a capillary for the admission of air. When the substance had completely volatilised and the vapour obeyed Charles's law, the pressure in *C* and the temperature were measured, the latter by means of a direct-reading platinum-resistance thermometer. The volume of *V* was measured after the experiment by filling it with water and weighing. The main source of error lies in the measurement of pressure when the substance is so unstable that fairly low pressures have to be used. The springs used in our experiments responded to pressure differences of about 1 mm.

*Results.—Phthalimide.* Weight : 62·0 mg. Volume : 39·4 c.c.

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Temp., K. | 478° | 533° | 543° | 568° | 583° | 603° | 613° | 603° | 593° |
| Pressure, mm. | 61 | 199 | 259 | 373 | 384 | 399 | 405 | 399 | 390 |
| $T/p$ | 7·8 | 2·7 | 2·1 | 1·52 | 1·515 | 1·51 | 1·51 | 1·51 | 1·515 |
| $M$ | — | — | — | 148 | 147·5 | — | 147 | — | — |

Mean $M$ = 147·5 between 295 and 340° (Calc. for $C_8H_5O_2N$: $M$, 147).

*Indigo.* Weight: 14·3 mg. Volume: 51·5 c.c.

| | | | | | | |
|---|---|---|---|---|---|---|
| Temp., K. | 648° | 668° | 688° | 703° | 688° | 658° |
| Pressure, mm. | 13 | 26 | 44 | 47 | 46 | 36 |
| $T/p$ | 49 | 25·7 | 15·6 | 15·0 | 15·0 | 18·3 |
| $M$ | — | — | — | 257 | — | — |

he estimated error in this measurement is $\pm$ 3·5%, mainly from a possible error of 2% in the ading of the pressure. Hence $M$ = 257 $\pm$ 9 (Calc. for $C_{16}H_{10}O_2N_4$ : $M$, 262).

*Phthalonitrile polymeride.* Trial experiments showed that the polymeride was undecomposed uring 5—10 minutes at 400—450°, but began to char on longer heating. Preliminary readings f pressure were therefore made after 1-minute immersions in the bath, preheated to the required emperature, an excess of the solid being used. The vapour pressures then exerted were 36—37 m. at 420°, 42 mm. at 425°, and 49 mm. at 430°. For the final readings a quantity of the solid as taken which exerted less than these pressures when fully volatilised.

Weight: 11·7 mg. Volume: 47·7 c.c. At 691° K. the pressure was 24 mm.; and was nchanged at 703° K. The estimated error is 6·25%, mainly from a possible error of 4% in the eading of pressure. Mean $M$ = 396 $\pm$ 25 [Calc. for $(C_8H_4N_2)_3$ : $M$, 384].

At 430°, but not noticeably at 420°, the trimeride was observed in two different apparatus to pass through the thin glass spring $B$ into the cool part of the upper chamber $C$. The sublimate was the pure polymeride, m. p. 296°. The most likely explanation seems to be the development of a pin-hole or crack at 430°. The apparatus could, however, be kept at this temperature with a constant deflexion of the pointer when there was a 20 mm. difference in pressure between the upper and lower chambers. This shows that, whatever the cause of the migration of material, it cannot affect the measurements of pressure.

The trimeride (5 g.) was dissolved in concentrated nitric acid (70 c.c.) at 100°, and kept for 2 days at room temperature. It was then diluted with 200 c.c. of water and kept for a further 3 days. An excellent yield of crystalline phthalimide (m. p. 229°, 4·25 g.) was obtained.

We are much indebted to Dr. R. H. Purcell for his assistance and advice in the construction of the apparatus.

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London, S.W.7. [Received, March 17th, 1938.]

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## 132. *The Hydrogenation of Simple Sulphur Compounds. Part I. Nickel Subsulphide as a Catalyst.*

By Roland H. Griffith and Samuel G. Hill.

Nickel subsulphide, $Ni_3S_2$, is a catalyst for the hydrogenation of the simple sulphur compounds which are present in small amounts in purified coal gas. The formation of this sulphide from metallic nickel, by way of the normal sulphide, has been investigated and the adsorption on it of carbon disulphide, carbon oxysulphide, methylthiol, sulphur dioxide, and hydrogen has been measured up to 350°.

In the hydrogenation of carbon disulphide, Evans and Stanier (*Proc. Roy. Soc.*, 1924, *A*, **105**, 626) showed that nickel subsulphide, $Ni_3S_2$, was a useful catalyst at temperatures about 420°. Renewed attention has recently been directed to the hydrogenation of carbon disulphide, carbon oxysulphide, methylthiol, and sulphur dioxide by the discovery (Hutchison, *Inst. Gas Eng.*, 1937, Publication 175, p. 8) that sulphur compounds more volatile than carbon disulphide are present in purified coal gas, and that nickel catalysts can be prepared which are active for their decomposition at temperatures from 150° upwards (Griffith, *ibid.*, p. 45).

The reactions occurring during the formation of the active catalyst and the adsorption of the reactants on it have been surveyed and are now summarised; more detailed studies of the individual hydrogenation reactions will be described in subsequent communications.

### Experimental.

Nickel hydroxide was prepared by precipitation from nickel chloride solution with sodium hydroxide, and washed completely free from chloride. Carbon disulphide was of A.R. quality; carbon oxysulphide was prepared by the interaction of ammonium thiocyanate and sulphuric acid (Moser, "Die Reindarstellung von Gasen," 1920, p. 120), condensed by acetone–solid carbon dioxide, and finally purified by fractionation to b. p. $-48°$; methylthiol was obtained by mild hydrogenation of carbon disulphide with a deficiency of hydrogen, followed by

fractionation to b. p. 6°. These distillations were carried out by Gooderham's method (*J. Soc. Chem. Ind.*, 1937, **56**, 32T). Sulphur dioxide was obtained from the liquid. All reagents and gases were dried when necessary by means of calcium chloride and phosphoric oxide; electrolytic hydrogen was purified by treatment with chromous chloride solution and drying.

*The Action of Carbon Disulphide and Sulphur Dioxide on Nickel.*—Nickel hydroxide was formed into small pellets about 0·15″ in diameter and 0·25″ long by the method of Griffith and Hill (*Trans. Faraday Soc.*, 1937, **33**, 405), and was reduced in a stream of hydrogen at 350° for 2 hours. The product was highly pyrophoric and was therefore never exposed to air.

The metallic nickel so obtained was converted into the sulphide by the action of carbon disulphide vapour carried in nitrogen for 3 hours at 350° (100 c.c./min. of nitrogen, with carbon disulphide at about 250 mm. pressure), or similarly carried by hydrogen. The products obtained by treatment of the reduced nickel with sulphur dioxide and with mixtures of sulphur dioxide and hydrogen were also examined, and the analyses of the different products are shown in Table I.

TABLE I.

| Source of material. | Ni, %. | S, %. | C, %. | O, %. |
|---|---|---|---|---|
| $Ni + CS_2 + N_2$ at 350° | 60·2 | 35·0 | 4·8 | — |
| Calc. for $NiS + \frac{1}{2}C$ | 60·6 | 33·2 | 6·2 | — |
| $Ni + CS_2 + H_2$ at 350° | 60·2 | 37·5 | 2·2 | — |
| ,, excess $H_2$ | — | — | 0·7 | — |
| ,, subsequently reduced | 67·2 | 26·0 | 6·8 | — |
| Calc. for $Ni_3S_2 + 1\frac{1}{2}C$ | 68·2 | 24·8 | 7·0 | — |
| $Ni + SO_2$ at 350° | 72·5 | 12·5 | — | 15·0 |
| Calc. for $2NiO + NiS$ | 73·3 | 13·3 | — | 13·4 |
| $Ni + SO_2 + H_2$ at 350° | 63·2 | 27·1 | — | 9·7 |
| Ni + coal gas, 21 days at 250° | 72·5 | 24·4 | 3·1 | — |

In practice, for the treatment of coal gas, the catalyst was prepared by reduction of nickel hydroxide at 350°; after contact with coal gas for several weeks it was found to be chiefly in the form of nickel subsulphide, as shown by the analysis included above. Methods of preparation of nickel sulphide involving precipitation from aqueous solution were not adopted in view of the results of Middleton and Ward (J., 1935, 1459), who showed that the isolation of pure products by such means was extremely difficult.

Attempts were made to measure the rate of reaction of carbon disulphide with evacuated metallic nickel, with the results given in Table II, but these figures are only very approximate owing to the large evolution of heat. At low temperatures, for instance, a definite acceleration of the reaction could be detected after a period of a few seconds, which must be attributed to a rise in temperature of the solid. When carbon disulphide was admitted to a small quantity of reduced nickel packed round a thermocouple at 20°, a rapid rise in temperature to 200° was observed, which ceased on cutting off the supply of carbon disulphide.

The results in Table I show that nickel decomposes carbon disulphide with the formation of nickel sulphide and carbon and that when hydrogen is present the formation of carbon is reduced, practically none being deposited with excess of hydrogen. The carbon once formed, however, does not react with hydrogen subsequently brought into contact with it at 350°, although decomposition of nickel sulphide occurs under these conditions, as described below.

In contact with sulphur dioxide, nickel is converted into a mixture of oxide and sulphide as found by Neogi and Adhicary (*Z. anorg. Chem.*, 1910, **69**, 209), but when hydrogen is also present, the oxide is reduced, while the sulphur content is only diminished towards that required by formation of the subsulphide.

TABLE II.

*Velocity of reaction of carbon disulphide with nickel at* 200°.

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Time (secs.) | 15 | 25 | 35 | 45 | 60 | 75 | 90 | 2220 |
| $CS_2$ vapour taken up, c.c./g. of Ni | 107·5 | 116 | 118 | 125 | 126 | 133 | 134 | 141 |

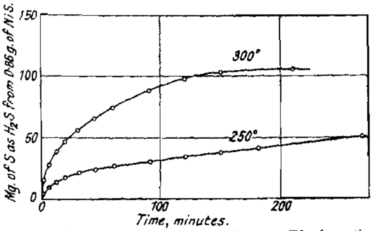
*The Action of Hydrogen on Nickel Sulphide.*—Although Evans and Stanier showed that reduction of nickel sulphide to $Ni_3S_2$ took place at 420°, it appeared desirable to measure the rate of reaction of hydrogen with the sulphide produced under the present conditions. The mixture of carbon and sulphide resulting from the action of carbon disulphide on nickel, as shown above, was therefore heated in a hard-glass tube at 350° for 20 hours in nitrogen to remove adsorbed carbon disulphide, and then treated with pure dry hydrogen (100 c.c./min.)

at 250° and 300°, the rate of hydrogen sulphide formation being determined. The results obtained are shown in Fig. 1 and it is clear that the subsulphide $Ni_3S_2$ is formed, and is produced rather more quickly at 300° by this method than was previously found by Evans and Stanier (*loc. cit.*) at 420°. The action of hydrogen on $Ni_3S_2$ at 300° is very slow.

Specimens of $Ni_3S_2$ used in adsorption measurements were prepared by reduction of NiS in hydrogen at 300° for 3 hours; the progress of the reduction was checked by determination of hydrogen sulphide in the exit gas. The solid was cooled in pure nitrogen to room temperature.

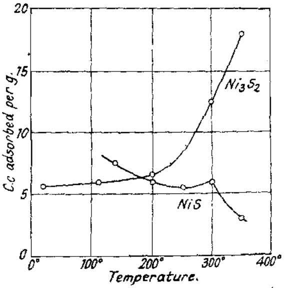
*Adsorption on Nickel Subsulphide.*—Griffith, Hill, and Plant's apparatus (*Trans. Faraday Soc.*, 1937, **33**, 1419) was used for measurement of adsorption. The weight of sulphide used was about 0·2 g., and it was exhausted to below 0·001 mm. pressure for at least 8 hours at 350°. Every sample was then cleaned by admission of a little hydrogen at 350°, followed by renewed evacuation. A fresh specimen, from a single preparation, was taken for each reagent investigated. Measurements were generally carried out at temperatures rising from 20° to 350°, and where the results showed any interest, the determinations were repeated after evacuation. Velocity measurements were also carried out in certain cases.

FIG. 1.



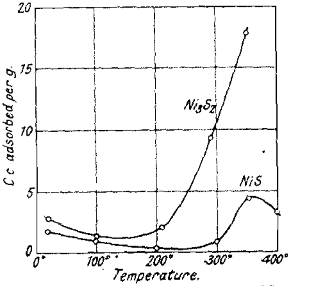

*Rate of decomposition of* NiS *by hydrogen. The formation of* $Ni_3S_2$ *requires the removal of* 102 *mg. from* 0·86 *g. of* NiS.

FIG. 2.




*Isobars at* 65—70 *mm. pressure for adsorption of* $CS_2$ *on nickel sulphides.*

FIG. 3.




*Isobars at* 65—70 *mm. for adsorption of* $SO_2$ *on nickel sulphides.*

In Figs. 2 and 3 are shown isobars for the adsorption of carbon disulphide and sulphur dioxide on $Ni_3S_2$ and, for comparison, also on NiS; in Table III are given the results obtained with hydrogen, carbon oxysulphide, and methylthiol.

TABLE III.

*C.c. of gas adsorped per g. of* $Ni_3S_2$.

| Temp.: | 20°. | 100°. | 150°. | 200°. | 250°. | 300°. | 350°. |
|---|---|---|---|---|---|---|---|
| Hydrogen | 0·29 | 0·49 | — | 0·61 | — | 0·59 | 1·08 |
| $CH_3$·SH | 2·06 | 0·76 | 0·36 | 0·17 | 0·32 | 0·08 | 0·0 |
| COS | 0·94 | 0·15 | — | 0·02 | — | 0·0 | — |

From the adsorption measurements, the information summarised below has been obtained:

*Carbon disulphide.* On nickel sulphide adsorption is extensive and reversible, having measurable velocities throughout the temperature range explored and also showing van der Waals adsorption at the lower temperatures. On the subsulphide extensive adsorption also occurs, but a slow reaction takes place, and repeated adsorptions after evacuation approach the lower values given by the normal sulphide. Examples of the changes are given by the velocity measurements of Table IV. Isobars obtained when the adsorption is irreversible are characterised by an unbroken rise with temperature, so that the inflexion generally shown by activated adsorption is absent.

TABLE IV.

*Velocity of* $CS_2$ *adsorption on* $Ni_3S_2$.

| Time (mins.) | Adsorption, c.c. of $CS_2$ vapour per g. of $Ni_3S_2$. 200°. | 200° (repeated). | 300°. | 300° (repeated). |
|---|---|---|---|---|
| 1 | 2·8 | 0·7 | 2·4 | 0·1 |
| 25 | 4·7 | 2·0 | 5·2 | 1·3 |
| 50 | 5·4 | 2·6 | 6·1 | 1·9 |
| 100 | 6·4 | 3·2 | 7·3 | 2·5 |
| 150 | 7·0 | 3·9 | 8·2 | 3·1 |

*Hydrogen.* Although the amounts involved are very much smaller than the quantity of carbon disulphide taken up, it is evident that activated adsorption begins between 100° and 200° on $Ni_3S_2$. The behaviour of NiS towards hydrogen is, of course, obscured by the formation of hydrogen sulphide at about 200—250°.

*Sulphur dioxide.* This gas is adsorbed normally by NiS, showing activated adsorption at 300° upwards; with the lower sulphide there is clear evidence for activated adsorption beginning about 200°, but the results are then complicated by slow decomposition of the solid and the adsorption is only partly reversible.

*Methylthiol.* Van der Waals adsorption predominates at temperatures below 200°, but activated adsorption sets in above this point. The amounts involved are small compared with those of carbon disulphide.

*Carbon oxysulphide.* Only very small adsorption could be detected at any temperature and there is no evidence for an activated type.

*Effect of Carbon on Adsorption.*—Measurements carried out on specimens of nickel sulphide prepared from carbon disulphide severally in the presence and in the absence of hydrogen showed that any carbon deposited at this stage was almost entirely without effect on the adsorption of carbon disulphide. A slight increase in the amount taken up at the lower temperatures was detectable when carbon was present, but this difference disappeared as the temperature rose.

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## 133. *The Hydrogenation of Simple Sulphur Compounds. Part II. Reactions of Carbon Disulphide and Sulphur Dioxide.*

By BLICK CRAWLEY and ROLAND H. GRIFFITH.

The hydrogenation of carbon disulphide with nickel subsulphide as the catalyst has been investigated at temperatures from 100° to 250°. The reaction is initially of the first order with respect to carbon disulphide, but is vigorously retarded by concentrations of this reagent such that hydrogen is still present in great excess.

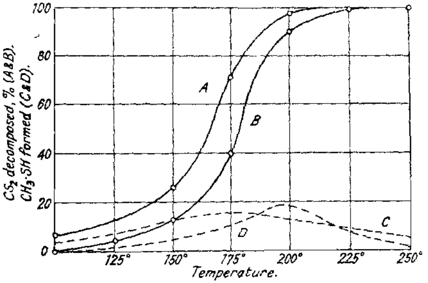
The hydrogenation of sulphur dioxide with the same catalyst is also of the first order with respect to that reagent, slight retardation appearing at the higher concentrations. These observations are compared with adsorption data previously described, and the significance of the formation of methylthiol from carbon disulphide is discussed.

THE formation of methylthiol by the catalytic hydrogenation of carbon disulphide is suggested by Sabatier's observations ("Katalyse," 1927, p. 107) although the product was

not identified. Evans and Stanier (*Proc. Roy. Soc.*, 1924, *A*, **105**, 626), on the other hand, concluded that the decomposition took place by formation of free carbon and hydrogen sulphide. Randall and Bichowsky (*J. Amer. Chem. Soc.*, 1918, **40**, 368) studied equilibria in the system $SO_2 + 3H_2 = 2H_2O + H_2S$, but no investigations have been described concerning the kinetics of either of these reactions, which form the subject of this communication.

*Hydrogenation of Carbon Disulphide.*—The catalyst used in these experiments was nickel subsulphide, $Ni_3S_2$, obtained as described in Part I (preceding paper). About 5 c.c. of catalyst space were used, or 1 c.c. at the highest temperatures, and the catalyst was heated electrically in a hard-glass tube, temperatures being measured by a platinum–platinum-rhodium couple embedded in it. The required mixtures of pure dry hydrogen and carbon disulphide vapour were prepared by use of the carburettor described by Chaplin and Cartwright (*J. Soc. Chem. Ind.*, 1937, **56**, 36T). The reaction products were examined for carbon disulphide, methylthiol, and hydrogen sulphide; the first was determined by alcoholic potash and iodine titration, the second as its silver compound after removal of hydrogen sulphide by iron oxide, and the last two together by silver nitrate. The rate of hydrogen passage was kept at 473 c.c./min., *i.e.*, 1 c. ft./hr., so that it was always present in great excess, and concentrations of sulphur compounds are expressed as mg. per c. ft., which is a convenient unit.

FIG. 1.




*Decomposition of* $CS_2$ *by hydrogen.*

A. *Initial* S *content* 8·0 *mg./c. ft.;* % *of* $CS_2$ *decomposed.*
B. ,, ,, 20·7 ,, ,, ,,
C. ,, ,, 8·0 ,, *thiol formed.*
D. ,, ,, 20·7 ,, ,, ,,

In Fig. 1 are shown the results at temperatures between 100° and 250°, and in the table are given some further calculations. No attempt was made to determine the order of the reaction with respect to hydrogen, as the catalyst would not persist as $Ni_3S_2$ under conditions where an excess of carbon disulphide was present. It may be noted that the content of sulphur generally contained in purified coal gas as carbon disulphide is between 12 and 24 mg. per c. ft.

From these results it is evident that the reaction initially approaches the first order with respect to carbon disulphide, but that retardation rapidly sets in as the concentration of that reactant is increased, and after the reaction passes through a stage of apparent zero order, this retardation becomes very pronounced. As the appearance of methylthiol and hydrogen sulphide follows the same course, the retardation cannot be due to those products but must be caused by carbon disulphide itself.

*Decomposition of carbon disulphide by hydrogen at* 175°.

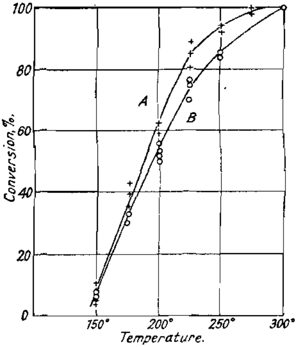
| Inlet $CS_2$, mg./hr. | $CS_2$ decomposed, %. | Total $CS_2$ decomp. per hr., mg. | $CH_3$·SH formed, mg./hr. | $H_2S$ formed, mg./hr. |
|---|---|---|---|---|
| 9·2 | 70 | 6·44 | 1·51 | 5·57 |
| 22·6 | 39 | 8·82 | 2·80 | 6·87 |
| 36·3 | 22 | 8·0 | 2·75 | 6·19 |
| 48·5 | | 3·9 | 1·84 | [illegible]·09 |

*Formation of Methylthiol.*—It has been found that the thiol is formed (1) at low temperatures as shown in the table, (2) at high temperature with a deficiency of hydrogen, or (3) at high temperatures with excess hydrogen and high space velocities. Although under condition (2) the catalyst will not remain wholly as $Ni_3S_2$ (see Part I), there is strong evidence from these observations that methylthiol is the primary hydrogenation product; other partly hydrogenated derivatives of carbon disulphide, such as thioformic acid or thioformaldehyde, cannot be isolated, and there is no evidence for the formation of free carbon.

Methylthiol can be conveniently prepared by passing hydrogen and carbon disulphide vapour in approximately equal volumes over nickel sulphide at 250—300°; 15 g. of catalyst will treat 200 c.c. of gas per minute. The products are freed from hydrogen sulphide by passage through iron oxide, and condensed by cooling with acetone–solid carbon dioxide, and the thiol is purified by fractionation as described in Part I.

In their study of the removal of sulphur compounds from naphtha by catalytic hydrogenation in the presence of nickel sulphide, Elgin, Wilder, and Taylor (*Ind. Eng. Chem.*, 1930, **22**, 1284) concluded that the process took place by formation of nickel sulphide and its reduction to nickel. The present results show that such a mechanism cannot apply to the hydrogenation of carbon disulphide with nickel subsulphide. If the rate-controlling step were the formation of NiS, retardation would not occur with higher carbon disulphide concentrations. Since this is the case, the rate of reaction would be controlled by the rate of reduction of NiS to $Ni_3S_2$. The maximum initial rate of formation of hydrogen sulphide from NiS can be calculated from the data of Part I as about 3 mg. per min. per g. of sulphide at 250°, whereas the rate of catalytic production of hydrogen sulphide from carbon disulphide at 250° was found to be only a few mg. per hour per g. of catalyst.

FIG. 2.




*Hydrogenation of* $SO_2$ *on* $Ni_3S_2$ *catalyst.*
A. *Inlet* S = 8·7 *mg./c. ft.*
B. „ 21·5 „

The results now described suggest that the reaction of carbon disulphide with hydrogen occurs in steps, leading to the formation of methylthiol as one of the intermediate products. The adsorption of both reagents is necessary for the primary reaction to take place, and the adsorption of the disulphide is so much more pronounced that it easily leads to complete covering of the catalyst surface and consequent retardation. In the further decomposition of the thiol formed, this substance also is adsorbed, but the kinetics of this reaction have not yet been investigated. Experiments with a smaller quantity of catalyst in the range 250—300° showed that the retarding effect of carbon disulphide persisted at the higher temperatures.

*Hydrogenation of Sulphur Dioxide.*—The catalyst was prepared and heated as before, and hydrogen (dried and oxygen free) was supplied at 1 c. ft. per hour. The required concentration of dry sulphur dioxide was obtained by mixing with the main stream a small measured portion (5—10 c.c./min.) of another stream containing 300 c.c./min. of hydrogen and 5—10 c.c./min. of the dioxide. This procedure was adopted to avoid the measurement of very small rates of flow of the latter gas. The content of dioxide at the inlet to the reaction tube was checked at frequent intervals.

The outlet gas was led into excess of N/10-iodine solution, and the amounts of sulphur dioxide and hydrogen sulphide were determined by titration with thiosulphate and with alkali. No trace of sulphur was observed to separate at any stage of the investigation.

In Fig. 2 are shown the results at temperatures between 100° and 300°. It is clear that the reaction is of first order with respect to sulphur dioxide, with very slight but definite retardation at the higher concentration. This conclusion also agrees with the observations of adsorption of sulphur dioxide on the catalyst described in Part I, where the amount taken up was shown to be very much larger than the volume of hydrogen adsorbed, but somewhat smaller than was the case with carbon disulphide.

From the foregoing results it appears that excessive adsorption of one reactant on a catalyst is generally an undesirable condition, and an improved catalyst would be one on which relatively less extensive adsorption of such a reagent took place.

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# 134. *Formation of the Indene Nucleus. Part III.*

By (the late) (MRS.) O. BLUM-BERGMANN.

1 : 3-*Diphenyl*-2-p-*anisylpropane*-2 : 3-*diol* (I), on dehydration, gives in fair yield 1-*phenyl*-2-p-*anisylindene* (II) according to a mechanism discussed in previous papers. The isomeric 1 : 2-*diphenyl*-3-p-*anisylpropane*-2 : 3-*diol* (III) gives no indene derivative under analogous conditions.

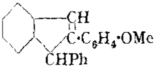
The synthesis of 1 : 3-*diphenyl*-2 : 3-*dimethylhydrindene* (IV) and 1-*phenyl*-2-*benzyl*-1-*methylhydrindene* (V) is reported. A substance previously described by Koelsch as (II) proves to be the isomeric 3-*phenyl*-2-*anisyl* compound (II*a*).

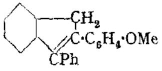
IT has been shown previously (*Ber.*, 1932, **65**, 109; J., 1935, 1020) that alkylhydrobenzoins may be converted by two-fold dehydration into β-arylindenes. The reaction does not occur regularly and the factors governing the possible dehydration processes are not yet clear. Experiments with a pair of structural isomerides which behave differently are now reported. 1 : 3-*Diphenyl*-2-p-*anisylpropane*-2 : 3-*diol* (I), easily prepared from phenyl-*p*-anisoylcarbinol and benzylmagnesium chloride, is partly monoacetylated (compare Orékhoff, *Bull. Soc. chim.*, 1919, **25**, 109; Cobler, Thesis, Berlin, 1932, p. 18) by boiling acetyl chloride, and partly dehydrated to form 1-*phenyl*-2-p-*anisylindene* (II). Pinacolinic rearrangement does not occur under the influence of acetyl chloride, but one of the rearrangement products was obtained directly in the preparation of (I). As, according to Tiffeneau and Lévy (*Bull. Soc. chim.*, 1931, **49**, 1617, 1661), benzylhydrobenzoin loses its secondary hydroxyl on rearrangement and as anisyl migrates in preference to benzyl, this *product* should be (I*a*).

$CH_2Ph \cdot C(OH)(C_6H_4 \cdot OMe) \cdot CHPh \cdot OH$
(I.)

$CH_2Ph \cdot CO \cdot CHPh \cdot C_6H_4 \cdot OMe$
(I*a*).

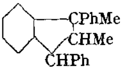
$CH_2Ph \cdot CPh(OH) \cdot CH(OH) \cdot C_6H_4 \cdot OMe$
(III.)

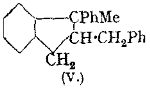

(II.)

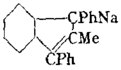

(II*a*.)

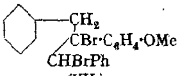
The isomeric 1 : 2-*diphenyl*-3-p-*anisylpropane*-2 : 3-*diol* (III), on the other hand, gave no indene derivative on treatment with boiling acetyl chloride or with phosphoric oxide in boiling benzene, rearrangement taking place. Besides the rearranged substance, which proved identical with the ketone (I*a*), a product isomeric with (III) was obtained; its structure could not be elucidated and it may be the hydrate of a second rearrangement product.

For comparison purposes in similar investigations, 1 : 3-*diphenyl*-2 : 3-*dimethylhydrindene* (IV) and 1-*phenyl*-2-*benzyl*-1-*methylhydrindene* (V) were synthesised by the following methods: (1) The easily accessible 3-phenyl-2-methylindone gave with phenylmagnesium bromide the expected carbinol; this was etherified and treated with sodium


(IV.)


(V.)


(VI.)


(VII.)

metal, the cleavage product (VI) methylated, and the resulting 1 : 3-*diphenyl*-2 : 3-*dimethylindene* hydrogenated, giving (IV). This synthesis is completely analogous to

that of the "dimeric *as*-diphenylethylene" described by Bergmann and Weiss (*Annalen*, 1930, **480**, 49). (2) From ββ-diphenylbutyric acid, 3-phenyl-3-methyl-1-hydrindone was obtained; its *benzylidene* derivative, on reduction with amalgamated zinc and hydrochloric acid gave (V) directly. This is remarkable, as Borsche (*Ber.*, 1919, **52**, 2077) had observed large resinification on Clemmensen reduction of simpler αβ-unsaturated ketones (compare Dippy and Lewis, *Rec. Trav. chim.*, 1937, **56**, 1001).

*Remarks on* 1-*Phenyl*-2-p-*anisylindene* (II).—Koelsch (*J. Amer. Chem. Soc.*, 1936, **58**, 1331) assigned formula (II) to a substance, m. p. 120—122°, which he obtained by decomposition of the dibromide (VII). This reaction, however, in the case of the methoxyl-free compound, is known to give a substance containing a methylene group (Orékhoff, *Chem. Zentr.*, 1923, I, 1620; Blum-Bergmann, J., 1935, 1020), so formula (II*a*) would be preferable for Koelsch's compound. The close relationship between our substance (m. p. 188—188·5°) and that of Koelsch is shown by the fact that they both give, in alkaline solution, the same benzylidene derivative, one of the starting materials undergoing allylic rearrangement (II → II*a*). That this applies to the isomer, m. p. 188—188·5°, follows from the observation that it is isomerised into the lower-melting product by sodium ethoxide, a reaction which is known to produce isomers containing a methylene group in similar cases.

## Experimental.

1 : 3-*Diphenyl*-2-p-*anisylpropane*-2 : 3-*diol* (I).—When phenyl-*p*-anisoylcarbinol (24·2 g.), m. p. 106° (Tiffeneau and Lévy, *Compt. rend.*, 1931, **192**, 287; *Bull. Soc. chim.*, 1931, **49**, 725), was added in small portions to an ethereal solution of benzylmagnesium chloride (7·3 g. of magnesium; 38·1 g. of benzyl chloride, *i.e.*, 3 mols.), a vigorous reaction took place and the product quickly crystallised. The mixture was boiled for 4 hours and decomposed with ice and dilute sulphuric acid, whereupon most of the dihydroxy-compound separated spontaneously, contaminated by one of the possible rearrangement products. They were separated by fractional crystallisation from benzene–light petroleum. The *dihydroxy-compound* (I) crystallised first in colourless needles (10 g. from 15·7 g. of the crude product) and was recrystallised from propyl alcohol or glacial acetic acid; m. p. 155—156·5° (Found: C, 79·0; H, 6·7. $C_{22}H_{22}O_3$ requires C, 79·0; H, 6·6%). Then white clusters appeared, which, on recrystallisation from glacial acetic acid, formed prisms, m. p. 134—135·5° (Found: C, 83·5; H, 6·5. $C_{22}H_{20}O_2$ requires C, 83·5; H, 6·3%). The ethereal solution, after separation of the solid phase, was evaporated; from the oily residue, on trituration with alcohol, 2·85 g. of the diol were isolated.

*Dehydration of* (I).—When the foregoing glycol (3 g.) was boiled with acetyl chloride (30 c.c.), the product partly crystallised. After 5 hours, the mixture was cooled, and the solid filtered off and washed with light petroleum (yield, 1·63 g.). The substance, which analysis indicated to be a *monoacetyl* derivative of (I), was recrystallised from propyl alcohol, then from glacial acetic acid until the m. p. was constant at 178—179·5°. It gave the same orange-red reaction with sulphuric acid as the diol (I) itself (Found: C, 76·6; H, 6·4. $C_{24}H_{24}O_4$ requires C, 76·6; H, 6·4%).

The filtrate from this substance, on removal of the excess of acetyl chloride, gave 1-*phenyl*-2-p-*anisylindene* (II) (0·85 g.); it was recrystallised from methyl ethyl ketone, then from glacial acetic acid, and formed colourless needles, which gave a yellow liquid at 188—188·5° (Found: C, 88·7; H, 6·0. $C_{22}H_{18}O$ requires C, 88·6; H, 6·0%).

1 : 2-*Diphenyl*-3-p-*anisylpropane*-2 : 3-*diol* (III).—The necessary benzoyl-*p*-anisylcarbinol was prepared from anisaldehyde cyanohydrin (Knorr, *Ber.*, 1904, **37**, 3172) and phenylmagnesium bromide by the method of McKenzie and Luis (*Ber.*, 1932, **65**, 794). The m. p. of our preparation was 88—89°, which is also given by Asahina and Terasaka (*Chem. Zentr.*, 1923, II, 434) and Jenkins (*J. Amer. Chem. Soc.*, 1933, **55**, 3048; 1934, **56**, 682); McKenzie and Luis (*loc. cit.*), McKenzie, Luis, Tiffeneau, and Weill (*Bull. Soc. chim.*, 1929, **45**, 414), and Arnold and Fuson (*J. Amer. Chem. Soc.*, 1936, **58**, 1295) give m. p. 100—101°. As our preparation gives the same yellow colour reaction with sulphuric acid as the substance, m. p. 100—101° (Luis, J., 1932, 2547), they are dimorphic forms rather than isomerides (*p*-anisoylphenylcarbinol has m. p. 106° and gives a green colour in sulphuric acid).

From 10 g. of anisaldehyde cyanohydrin, 8·5—8·7 g. of benzoyl-*p*-anisylcarbinol were obtained, which crystallised from ligroin or dilute alcohol in prismatic needles, m. p. 88—89° (Found: C, 74·5; H, 5·9; OMe, 13·0. Calc. for $C_{15}H_{14}O_3$: C, 74·4; H, 5·8; OMe, 12·8%).

It was characterised by its *oxime* (1 g. of the carbonyl compound in 5 c.c. of alcohol boiled with 0·7 g. of hydroxylamine hydrochloride and 0·4 g. of sodium hydroxide in water for 3 hours), which separated from benzene in silky needles containing about 0·5 mol. of benzene (Found: $C_6H_6$, 15·2. $C_{15}H_{15}O_3N,0·5C_6H_6$ requires $C_6H_6$, 13·0%). The benzene-free oxime had m. p. 121—122·5° (Found: N, 5·4; OMe, 12·4. $C_{15}H_{15}O_3N$ requires N, 5·4; OMe, 12·1%).

Benzoyl-*p*-anisylcarbinol (1 g.) was isomerised quantitatively within 4 hours by boiling glacial acetic acid (3 g.) containing concentrated hydrochloric acid (2 g.). The mixture was poured into water, and the *p*-anisoylphenylcarbinol extracted with ether and crystallised from alcohol; m. p. and mixed m. p. 106° (for other means of isomerisation, see Luis, J., 1932, 2547; Julian and Passler, *J. Amer. Chem. Soc.*, 1932, **54**, 4756; Buck and Ide, *ibid.*, 1933, **55**, 855).

Benzoyl-*p*-anisylcarbinol (6·1 g.) was added to an ethereal solution of benzylmagnesium chloride (prepared from 1·82 g. of magnesium and 9·48 g. of benzyl chloride). After 5 hours' boiling, the mixture was decomposed with cold dilute sulphuric acid, and the ethereal solution, to which ethyl acetate was added in order to prevent spontaneous crystallisation, evaporated. The solid residue (7·5 g.) crystallised from alcohol in prisms, m. p. 161—163°, of 1 : 2-*diphenyl*-3-p-*anisylpropane*-2 : 3-*diol* (Found: C, 79·2; H, 6·7; OMe, 9·1. $C_{22}H_{22}O_3$ requires C, 79·0; H, 6·6; OMe, 9·3%).

*Dehydration.* The dihydroxy-compound (*III*) (2·5 g.) was dissolved in boiling benzene (35 c.c.), and phosphoric oxide (1·5 g.) added in small portions. The vigorous reaction produced a light brown, resinous mass, which was treated with ether and ice-water. The oily product was distilled in a vacuum (b. p. 255—259°; yield, 2·1 g.) and then triturated with alcohol. Slow fractional crystallisation from light petroleum gave brilliant prisms (A) and white needles (B), which were separated mechanically. The prisms (A), after recrystallisation from alcohol or light petroleum, had m. p. 48—49·5°; analysis pointed to the formula $C_{22}H_{22}O_3$ (Found: C, 78·9; H, 6·5; OMe, 10·0; *M*, in camphor, 323, 310. Calc.: C, 79·0; H, 6·6; OMe, 9·3; *M*, 334). The needles (B) crystallised well from propyl alcohol or glacial acetic acid; m. p. and mixed m. p. with the product described on p. 724, 134—135° (Found: C, 83·4; H, 6·5; OMe, 9·8. Calc. for $C_{22}H_{20}O_2$: C, 83·5; H, 6·3; OMe, 9·9%). Acetyl chloride gave the same products as treatment with phosphoric oxide.

αβ-*Dimethylcinnamic Acid*.—This was prepared by Rupe, Steiger, and Fiedler's method (*Ber.*, 1914, **47**, 63; compare Burton and Shoppee, J., 1935, 1156; Ruzicka and Ehmann, *Helv. Chim. Acta*, 1932, **15**, 140) from acetophenone, ethyl α-bromopropionate, and zinc. The ester, obtained by treating the crude condensation product with 3 vols. of 85% formic acid (3 hours at 150°), had b. p. 134—136°/18 mm. The acid, prepared by means of methyl-alcoholic potash, had b. p. 169°/16 mm. and crystallised spontaneously, forming a mass melting at 57—67°. It can be separated into the pure *cis-trans*-isomers by crystallisation from light petroleum (b. p. 80—100°): from 0·5 g. of the mixture there separates 0·13 g. of thin needles, which after recrystallisation from the same solvent have m. p. 108·5—110° (Found: C, 74·9; H, 7·0. Calc. for $C_{11}H_{12}O_2$: C, 75·0; H, 6·8%); the mother-liquor of the 0·13 g. leaves, on evaporation, hexagons, which are conveniently recrystallised from 20% acetic acid, forming plates, m. p. 105—107° (Found: C, 75·1; H, 6·9%).

ββ-*Diphenyl*-α-*methylbutyric Acid*.—The mixture of isomeric αβ-dimethylcinnamic acids (19·5 g.) was dissolved in benzene (250 c.c.) and, after addition of powdered aluminium chloride (17 g.), kept at room temperature for 7 days; the brown mass was then decomposed with ice and concentrated hydrochloric acid. The benzene layer was extracted with sodium carbonate solution and evaporated; the residue, after trituration with and recrystallisation from light petroleum (b. p. 40—80°), gave 2 : 3-dimethylindone (1·3 g.), m. p. 78—79°. On acidification, the alkaline extract gave a viscous oil, which was isolated by ether extraction and triturated with light petroleum (b. p. 80—100°). The ββ-*diphenyl*-α-*methylbutyric acid* thus obtained crystallised from 70% acetic acid or 70% methyl alcohol in prismatic needles (10·3 g.), m. p. 124—126° (Found: C, 80·3; H, 7·2. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%). The light petroleum mother-liquor contained an oil, which after distillation (b. p. 167—175°/15·5 mm.) crystallised spontaneously (yield, 5·5 g.); it was recrystallised from 50% acetic acid, forming leaflets, m. p. 132—133·5°. The analysis showed that, under the influence of aluminium chloride, partial transfer of hydrogen had taken place (compare Pummerer and Binapfl, *Ber.*, 1921, **54**, 2768; 1922, **55**, 3095), β-phenyl-α-methylbutyric acid (Rupe, Steiger, and Fiedler, *loc. cit.*) being formed (Found: C, 74·4; H, 8·1. Calc. for $C_{11}H_{14}O_2$: C, 74·1; H, 7·9%).

ββ-*Diphenyl*-α-*methylbutyryl chloride* (9·3 g.) was obtained from the acid (9·8 g.) and warm thionyl chloride (30 c.c.) and was immediately distilled; b. p. 188—189°/17 mm. (Found: C, 75·2; H, 6·5; Cl, 13·1. $C_{17}H_{17}OCl$ requires C, 74·8; H, 6·2; Cl, 13·0%).

*3-Phenyl-2 : 3-dimethyl-1-hydrindone.*—When powdered aluminium chloride (5·2 g.) was added in small portions to a solution of the foregoing chloride (9·3 g.) in carbon disulphide (30 c.c.), a vigorous reaction occurred; after 2 hours' boiling, the mixture was decomposed with cold hydrochloric acid, and the *hydrindone* obtained as a viscous oil (7·6 g.), b. p. 189—192°/16 mm. (Found : C, 86·5; H, 7·0. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8%). It was recovered mostly unchanged after treatment with phenylmagnesium bromide and therefore could not be utilised for the preparation of (IV).

1 : *3-Diphenyl-2-methyl-1-indenol.*—An ethereal solution of phenylmagnesium bromide (from 4·9 g. of magnesium and 20·9 c.c. of bromobenzene) and 3-phenyl-2-methylindone (22 g.) (Bergmann and Weiss, *Annalen*, 1930, **480**, 73) was boiled for 2 hours, and the crystalline cake decomposed with ice and ammonium chloride. The crude carbinol (34 g.), which would not crystallise, was boiled for 4 hours with methyl alcohol (340 c.c.) and concentrated hydrochloric acid (17 c.c.), most of the solvent distilled off (250 c.c.), and the residue treated with water and ether. The *methyl* ether crystallised spontaneously after distillation (b. p. 215—220°/10 mm.). It was triturated with methyl alcohol and recrystallised from alcohol, forming prisms (18·8 g.), m. p. 71—72·5°. With concentrated sulphuric acid it gave a brown-red colour (Found : C, 88·8; H, 6·5. $C_{23}H_{20}O$ requires C, 88·5; H, 6·4%).

1 : *3-Diphenyl-2 : 3-dimethylindene* (VI, with Me instead of Na).—The foregoing ether (5 g.) in ethereal solution was shaken with sodium powder for 3 days, lemon-yellow, silky needles of the sodium compound (VI) separating. After addition of an excess of methyl iodide (6 c.c.) the colourless ethereal solution was washed with water, dried, and evaporated, and the residue triturated with alcohol and recrystallised from the same solvent or from light petroleum (b. p. 40—60°), forming cubic crystals (3·9 g.), m. p. 68·5—69·5° (Found : C, 93·4; H, 6·9. $C_{23}H_{20}$ requires C, 93·2; H, 6·8%).

1 : *3-Diphenyl-2 : 3-dimethylhydrindene* (IV).—The foregoing hydrocarbon (3 g.) was catalytically hydrogenated in boiling propyl alcohol (15 c.c.) in presence of palladised barium sulphate (1·5 g.) for 6 hours. The solvent was evaporated, and the residue triturated with alcohol. 1 : *3-Diphenyl-2 : 3-dimethylhydrindene* separated from the same solvent or from glacial acetic acid in octahedra (2·1 g.), m. p. 97·5—98·5° (Found : C, 92·7; H, 7·5; *M*, in camphor, 310, 328. $C_{23}H_{22}$ requires C, 92·6; H, 7·4%; *M*, 298). The mother-liquor contained a viscous oil, b. p. 222—223°/10 mm., which may have contained isomeric forms of the crystalline hydrocarbon but was not investigated.

*2-Benzylidene-3-phenyl-3-methyl-1-hydrindone.*—A mixture of 3-phenyl-3-methyl-1-hydrindone (1·1 g.) (Blum-Bergmann, *Ber.*, 1932, **65**, 118) and benzaldehyde (0·53 g.) was dissolved in alcohol (20 c.c.) at 50°, and 25% alcoholic potassium hydroxide (5 drops) added. The brown mixture was kept at 0° for 2 days and then poured into water. The *product*, isolated by extraction with ether, crystallised spontaneously; recrystallised from methyl alcohol, it formed stout prisms (0·4 g.), m. p. 121—122° (Found : C, 89·3; H, 5·8. $C_{23}H_{18}O$ requires C, 89·0; H, 5·8%).

*1-Phenyl-2-benzyl-1-methylhydrindene* (V).—The preceding benzylidene derivative (1 g.) was boiled with amalgamated zinc wool (8 g.) and concentrated hydrochloric acid until the metal had dissolved. The *product* was extracted in ether, washed with sodium hydroxide solution, dried, and recovered. The residue crystallised on treatment with acetone and was recrystallised from propyl alcohol, forming long white needles (0·6 g.), m. p. 117—118·5° (Found : C, 92·2; H, 7·5. $C_{23}H_{22}$ requires C, 92·6; H, 7·4%).

*Experiments with 1-Phenyl-2-p-anisylindene* (II).—(a) The indene derivative (1 g.) was suspended in boiling propyl alcohol (50 c.c.), and sodium ethoxide solution and benzaldehyde added according to Koelsch's prescription (*loc. cit.*). The clear, reddish solution deposited, on standing, a bright yellow precipitate of the benzylidene derivative, which, after recrystallisation from propyl alcohol, formed needles, m. p. 192—193°, as reported by Koelsch.

(b) When a suspension of the indene derivative (0·5 g.) in propyl alcohol (10 c.c.) was treated with a solution of sodium (0·1 g.) in alcohol (2·5 c.c.), the temperature rose markedly and a clear solution was formed. On standing, the isomeric indene (II*a*) was precipitated; it separated from alcohol in silky needles, m. p. 120—121°, as stated by Koelsch (*loc. cit.*).

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# 135. *The Addition of Diphenylketen to Styrene.*

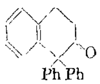
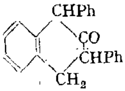
By Ernst Bergmann and (the late) (Mrs.) Ottilie Blum-Bergmann.

The addition product of diphenylketen and styrene is 2 : 2 : 3-triphenyl*cyclo*butan-1-one, since its hydrolytic fission gives β-benzhydryl-β-phenylpropionic acid.

In certain cases dimerisation products of ethylenes formerly regarded as *cyclo*butane derivatives have been proved to be formed by additive reactions involving migration of hydrogen or similar processes of greater complexity. As a matter of fact, only photochemical dimerisations seemed to lead to *cyclo*butane derivatives. Therefore, the formulation of the interaction between ketens and ethylenes, leading to *cyclo*butane compounds according to Staudinger and co-workers (*Ber.*, 1920, **53**, 1092; *Helv. Chim. Acta*, 1924, **7**, 8), *e.g.*,

| | | | | | | |
|---|---|---|---|---|---|---|
| $CPh_2$:CO<br>CHPh:$CH_2$ | $\longrightarrow$ | (A.) | $CPh_2$—CO<br>CHPh—$CH_2$ | or | (B.) | $CPh_2$—CO<br>$CH_2$—CHPh |

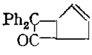
has been investigated, especially as no direct argument for the above structures has yet been advanced. In the case formulated above, Staudinger based his suggestion on the fact that the addition product, on treatment with alkali, takes up 1 mol. of water, giving a monobasic acid, $C_{22}H_{20}O_2$, which he regarded as ααγ-triphenylbutyric acid (I) or ααβ-*triphenylbutyric acid* (II). We are indebted to Prof. Staudinger for a sample of this acid.

| | | | | |
|---|---|---|---|---|
| $CPh_2$·$CO_2H$<br>$CH_2$·$CH_2$Ph | $CPh_2$·$CO_2H$<br>CHPhMe | $CPh_2$·OH<br>CHPhMe |  |  |
| (I.) | (II.) | (III.) | (IV.) | (V.) |

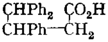
Neither of these formulæ is satisfactory. ααγ-Triphenylbutyric acid, although having nearly the same m. p. as Staudinger's acid (Schlenk and Bergmann, *Annalen*, 1930, **479**, 86) is different from it. The same holds for the acid (II), which we synthesised in the following way: α-methyldeoxybenzoin, by reaction with phenylmagnesium bromide, was converted into 1 : 1 : 2-*triphenylpropan*-1-*ol* (III), and the *methyl* ether of the latter was converted by the successive action of sodium and carbon dioxide into the acid (II). The method is unambiguous, as all the reactions were carried out under non-acidic conditions, so that no Wagner rearrangement was likely to occur (compare the case of diphenyl-*tert.*-butylcarbinol, Bateman and Marvel, *J. Amer. Chem. Soc.*, 1927, **49**, 2914; Conant and Bigelow, *ibid.*, 1928, **50**, 2041). We thought at first, therefore, that the addition of diphenylketen to styrene may involve reaction at a nuclear double bond of styrene or of diphenylketen, thus leading to the formation of (IV), (V), or some other substance analogous to these, in much the same way that occurs in the reactions between benzophenonephenylimide and phenylmagnesium bromide (Gilman, Kirby, and Kinney, *ibid.*, 1929, **51**, 2252), ethyl azodicarboxylate and styrene derivatives (Ingold and Weaver, J., 1925, **127**, 378; Diels and Alder, *Annalen*, 1926, **450**, 237) or *as*-diphenylethylene and maleic anhydride (Wagner-Jauregg, *Ber.*, 1930, **63**, 3218; *Annalen*, 1931, **491**, 1). A series of acids $C_{22}H_{20}O_2$ which could have been formed by hydrolytic fission of (IV), (V), and other analogously formed addition products has been synthesised, but none of them was identical with Staudinger's acid; the details of these experiments will be reported elsewhere.

Lewis, Ramage, Simonsen, and Wainwright (J., 1937, 1837) have proved that *cyclo*pentadiene gives with diphenylketen a four-membered ring (VI) and that under certain conditions it undergoes hydrolytic fission between the diphenylated carbon atom and the carbonyl group, and evidence pointing in the same direction has been put forward by Farmer (*Chem. and Ind.*, 1937, **56**, 1080) for the pairs diphenylketen and *cyclo*hexene and diphenylketen and *cyclo*hexadiene. In view of these findings we returned to the formulæ

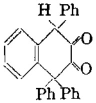
(A) and (B), this time considering other possibilities of hydrolytic fission than those leading to (I) and (II).



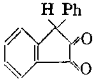
(VI.)



(VII.)



(XI.)



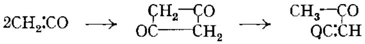
(XII.)

CHPh:CH·C($CHPh_2$)$_2$·OH (IX.)   CHPh:CH·CO·$CHPh_2$ (X.)

β-Benzhydryl-β-phenylpropionic acid (VII) proved to be identical with Staudinger's acid; for the original addition product of diphenylketen and styrene, therefore, formula (A) is valid.

The methyl ester of (VII) had been prepared by one of the present authors (J., 1936, 412) by interaction between benzhydrylsodium and methyl cinnamate (1 : 4-addition). Both the acid and the ester gave no depression in m. p. on admixture of Staudinger's acid and its methyl ester, respectively. A by-product of the above reaction has been obtained in which 2 mols of benzhydrylsodium are combined with 1 mol. of methyl cinnamate and which, therefore, most probably is dibenzhydrylstyrylcarbinol (IX). The same product was isolated from the analogous reaction with ethyl cinnamate, along with the *ethyl* ester of (VII). Its formation is due to addition of the organo-metallic compound to the ester group only.

Formula (B) is to be excluded for another reason. It could not account for the isomerisation into benzhydryl styryl ketone (X) of the original addition product, observed by Staudinger (*loc. cit.*), consisting in a hydrogen transfer and opening of the four-membered ring. A similar process may take place in the dimerisation of keten into acetylketen (Hurd and Williams, *J. Amer. Chem. Soc.*, 1936, **58**, 962), which involves intermediary formation of *cyclo*butanedione :



Why did Staudinger not take into account formula (VII) besides (II)? He was apparently misled by his observation that the acid $C_{22}H_{20}O_2$ on heating decomposes into styrene and diphenylacetic acid, so that the carboxyl group of the acid was likely to be connected with the diphenylated carbon atom. In fact this pyrolytic reaction of the acid has to be preceded by dehydration into (A); (A) decomposes into its generators styrene and diphenylketen, and the latter is hydrated to form diphenylacetic acid.

Although the " hetero-dimerisation " of diphenylketen and styrene does not involve nuclear double bonds, the cases quoted above show that such a possibility should not be completely disregarded. We are inclined to think that the dimeric diphenylketen of Langenbeck (*Ber.*, 1928, **61**, 938) is formed by such a reaction, the formula suggested by this author and even more the diradical structure proposed by Wittig and von Lupin (*ibid.*, p. 1627; compare Langenbeck, *Ber.*, 1929, **62**, 962) being rather improbable (compare Mueller, *Ber.*, 1935, **68**, 1883). The formula (XI) for the dimeric diphenylketen would account for the resemblance between it and 1-phenylindane-2 : 3-dione (XII), recently described by Koelsch (*J. Amer. Chem. Soc.*, 1936, **58**, 1321), both substances exhibiting, *inter alia*, the same potassium permanganate-like colour in the crystalline state.

## EXPERIMENTAL.

*ααβ-Triphenylbutyric Acid* (II).—Methyldeoxybenzoin was prepared from methylhydrobenzoin (30 g. and 240 g. of concentrated sulphuric acid gave 18 g., which crystallised from alcohol in needles, m. p. 53—55°) and converted into 1 : 1 : 2-*triphenyl-propane*-1-*ol* (III) (13 g. of the ketone with 2·3 g. of magnesium and 15 g. of bromobenzene) according to Lévy (*Bull. Soc. chim.*, 1921, **29**, 872, 893). The carbinol was recrystallised from light petroleum, forming monoclinic crystals (9 g.), m. p. 92—93° (Found : C, 87·3; H, 6·8. $C_{21}H_{20}O$ requires C, 87·5; H, 6·9%).

To a solution of the carbinol (4·5 g.) and methyl iodide (7 g.) in xylene (80 g.), potassium

(1·8 g.) was added in small portions. The mass was boiled for 3 hours; after the first hour, a second portion of methyl iodide (7 g.) was added. The last traces of metal were removed mechanically and the xylene solution was washed with water, dried, and evaporated. The crystalline residue of the *methyl* ether, recrystallised from light petroleum (b. p. 40—80°), had m. p. 98—99°; yield, 2 g. (Found: C, 87·8; H, 7·4. $C_{29}H_{22}O$ requires C, 87·4; H, 7·3%). The methyl ether (1 g.) was shaken with sodium metal in dry ether for several weeks, the excess of sodium removed by decantation, and the violet-red mass treated with carbon dioxide at 0°. The salt formed was dissolved in water, and the solution acidified; the precipitated *acid* (II) was dried and recrystallised from benzene; m. p. 158° (Found: C, 83·6; H, 6·5. $C_{22}H_{20}O_2$ requires C, 83·5; H, 6·4%).

*β-Benzhydryl-β-phenylpropionic Acid* (VII).—(*a*) To an ethereal solution of benzhydryl-sodium (from 10 g. of benzhydryl methyl ether), methyl cinnamate (8 g.) was added. After 12 hours' standing, the product was treated with dilute sulphuric acid, and the ethereal layer dried and evaporated. The oily residue, on trituration with light petroleum and acetone, yielded crystals, which separated from propyl alcohol in needles, m. p. 172° (IX) (Found: C, 89·8; H, 6·9; *M*, in camphor, 438. $C_{35}H_{30}O$ requires C, 90·0; H, 6·5%; *M*, 466). The mother-liquor of the crystals was distilled at 2 mm. The oil passing over at 205—210° crystallised spontaneously; m. p. 126°, as indicated before for the methyl ester of (VII).

*Hydrolysis.* The ester (0·5 g.) was dissolved in methyl alcohol (4 c.c.) and boiled with 15% methyl-alcoholic potash (6 c.c.; 10 mols.) for 3 hours. The product was diluted with water and acidified, and the precipitate recrystallised from 50% acetic acid; it formed needles, m. p. 178°. The mixture with Staudinger's acid had m. p. 178°.

(*b*) Starting with ethyl cinnamate (9 g.), the same observations were made. After removal of the product (IX), the oil was distilled in a vacuum; b. p. 200°/1 mm. The *ethyl* ester of (VII) crystallised on trituration with methyl alcohol; after recrystallisation from light petroleum, it had m. p. 83° (Found: C, 83·8; H, 7·2. $C_{24}H_{24}O_2$ requires C, 83·7; H, 7·0%).

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## 136. *Reaction Kinetics in Films. The Active Agents in the Aqueous Halogenation of Long-chain Phenols.*

By A. E. ALEXANDER.

The use of the monolayer technique of following the course of chemical changes has been extended to reactions between phenols and aqueous halogens which in the bulk phase take place much too rapidly to be measured by ordinary methods. *p*-Hexadecylphenol being used as the film-forming compound, the kinetics of reaction with aqueous iodine, bromine, and chlorine have shown that the active intermediaries are the hypohalous acid and the trihalide ion, the relative activities being HIO > HBrO > HClO, and $I_3' < Br_3' < Cl_3'$. These conclusions have been confirmed by experiments in the bulk phase.

THE monolayer method of following reaction kinetics allows reactions to be studied which in bulk occur too rapidly for measurement, and this work opens up a new method of approach to the study of very rapid reactions.

The reactivity of halogens in solution, both for addition reactions to unsaturated compounds and for substitution reactions with aromatic substances such as phenol and aniline, is well known to increase with the polarity of the solvent, being very small in carbon tetrachloride and extremely high in water, which suggests that the active intermediary is not the halogen molecule but one or more of the hydrolysis products formed according to the reaction $X_2 + H_2O \rightleftharpoons HXO + H^{\cdot} + X'$. In agreement with this, most reactions involving aqueous halogens are retarded by hydrogen ions (Baines, J., 1922, **121**, 2810; Moelwyn-Hughes, "Kinetics of Reactions in Solution," p. 203). Cofman (J., 1919, **115**, 1040) and Baines (*loc. cit.*) ascribed the activity entirely to the hypohalous acid, a view which was later rejected by Francis (*J. Amer. Chem. Soc.*, 1925, **47**, 2340), who showed that the reactions of pure aqueous hypobromous acid differed

from those of bromine-water. He therefore postulated bromine atoms, probably with positive charges, as the active intermediary, but a simple calculation from the known $Br_2 \rightleftarrows 2Br$ equilibrium (Bodenstein, *Z. Elektrochem.*, 1916, **22**, 327) shows that, unless the aqueous medium has an unexpectedly large effect on this equilibrium, the concentration of free atoms at room temperature is entirely negligible. Soper and Smith's kinetic study of chlorination and iodination of phenols (J., 1926, 1582; 1927, 2757) also showed quite definitely that the halogenating agent could not be the positive halogen ion, but in addition, indicated that some intermediary other than the hypohalous acid was involved. The main reasons why the hypohalous acid cannot be the sole active agent in halogenation are as follows: (*a*) Free chlorine-water reacts more rapidly with phenol than does hypochlorous acid alone (Soper and Smith, *loc. cit.*); (*b*) chlorine-water readily chlorinates phenolic ethers, whereas hypochlorous acid is entirely without effect (*idem, ibid.*); (*c*) aniline and hypobromous acid give grey and partly colloidal precipitates, whereas slightly acidified bromine-water gives a white precipitate of tribromoaniline (Francis, *loc. cit.*); (*d*) bromination by free bromine-water is about 1000 times as rapid as that with hypobromous acid (*idem, ibid.*); (*e*) gold leaf is dissolved readily in bromine-water but is unattacked by hypobromous acid (*idem, ibid.*); (*f*) mixed halogen addition products of unsaturated compounds are formed in salt solutions (*idem, ibid.*).

From this experimental evidence one is led to conclude that, although the hypohalous acid is without doubt an active halogenating agent, it cannot be the only one, and so, rejecting the positive halogen ion theory, a more probable intermediary has to be found.

The great difficulty in studying reactions with bromine-water has always been the very high velocities encountered, the reactions being complete in a few minutes even in extremely dilute solution. This has been overcome by using a monolayer of a long-chain phenol spread on a substrate of bromine-water of suitable concentration. From the rate of change of the surface pressure and surface potential, the reaction velocity can in general be calculated (Alexander and Rideal, *Proc. Roy. Soc.*, 1937, *A*, **163**, 70), even for reactions with half-life of the order of 40 seconds.

## Experimental.

The apparatus employed was identical with that previously described (Alexander and Rideal, *loc. cit.*). The chlorine- or bromine-water was made up shortly before use, and standardised against sodium thiosulphate after addition of potassium iodide. The substrate concentration was generally about $10^{-4}$M with respect to the total halogen and N/100 with respect to sulphuric acid. The latter ensured that both the phenol and the hypohalous acid were in the un-ionised form, so that there was no possibility of reactions involving either the phenoxide or the hypohalite ions. The hypohalous acid was prepared by Francis' method (*loc. cit.*, p. 2342), and standardised with potassium iodide and thiosulphate before and after use.

The phenol used, *viz.*, *p*-hexadecylphenol, was very kindly given by Professor N. K. Adam.

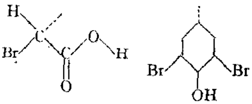
*Results.*—The films of the phenol were solid and stable up to quite high pressures (*ca.* 20 dynes/cm.), the *F–A* measurements and the hysteresis phenomena being in accord with the early measurements of Adam (*Proc. Roy. Soc.*, 1923, *A*, **103**, 676). The moment of the phenol (*ca.* 2·5 milli-Debyes) is somewhat greater than that of the alcohols (*ca.* 2·2 milli-Debyes), as would be expected owing to the presence of the benzene nucleus.

On injecting a few drops of saturated bromine-water beneath a film of the phenol at a constant surface pressure (2 dynes/cm. in all the experiments described below), a very rapid expansion was noticed, the apparent moment ($\mu$) increased very considerably, and the state of the film changed from solid to liquid, showing that bromination had taken place. The final area and moment were about 37 A.$^2$ and 3·55 milli-Debyes, as compared with the initial values of about 23·5 A.$^2$ and 2·5 milli-Debyes.

By analogy with the bulk bromination of *p*-cresol, it would be anticipated that substitution affords 2 : 6-dibromo-*p*-hexadecylphenol. This is substantiated by the dipole moment, which can be calculated very approximately from the effect of the introduction of bromine into other long-chain compounds. A comparison of the unsubstituted with the $\alpha$-bromo-acids (author's

ıpublished results) shows that the effect of the α-bromine atom is to increase μ by about 6 milli-Debye. Although the configuration of the acid dipole is still unsettled, yet, as will e seen from Fig. 1, it is very probable that the C–Br nkages are inclined at approximately the same angle ith respect to the surface in both cases, and on this ssumption the moment of the dibromophenol should e about 3·7 milli-Debyes, in fair agreement with the xperimental value previously quoted.

FIG. 1.




*Suggested probable configurations for the α-bromo-acid and dibromophenol dipoles.*

When the phenol was spread on a dilute bromine-ater substrate ($10^{-3}$ to $10^{-4}$M), the area–time curve as found to be unimolecular in shape, and the seudo-unimolecular velocity constant ($k_{uni}$) was cal-ulated from this curve by Guggenheim's method (*Phil. Mag.*, 1926, **2**, 538).

On addition of potassium bromide to the dilute bromine-water substrate, a very ronounced increase in the reaction velocity was noted, which suggested that the $Br_3'$ ion vas active in bringing about bromination. A series of experiments was therefore carried out n which a definite concentration of bromine ($0{\cdot}96 \times 10^{-4}$M) and various concentrations of potassium bromide were used. From the known values of the equilibrium constants of the two reactions

$$Br_3' \rightleftharpoons Br_2 + Br' \qquad K_1 = [Br_2][Br']/[Br_3'] \quad . \quad . \quad . \quad . \quad (1)$$

$$Br_2 + H_2O \rightleftharpoons H^{\bullet} + Br' + HOBr \qquad K_2 = [H^{\bullet}][Br'][HBrO]/[Br_2] \quad . \quad (2)$$

it is possible to calculate the concentrations of the various components ($Br_2$, $Br_3'$, $Br'$, and HOBr). If the total concentrations of bromine and of potassium bromide are respectively $c_1$ and $c_2$, then for the concentrations of bromide used in these experiments ($2{\cdot}5 \times 10^{-3}$—$0{\cdot}9$M), the following relations hold :

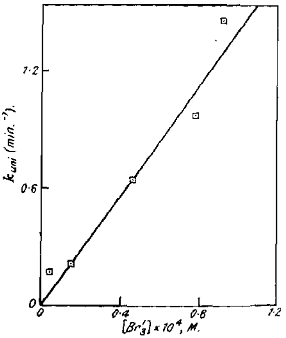
$$[Br_3'] = \tfrac{1}{2}\left\{(c_1 + c_2 + K_1) - \sqrt{(c_1 + c_2 + K_1)^2 - 4c_1c_2}\right\} \quad . \quad . \quad . \quad . \quad (3)$$

$$[Br'] = c_2 - [Br_3'] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$[Br_2] = c_1 - [Br_3'] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Taking $K_1$ from the data of Griffith, McKeown, and Winn (*Trans. Faraday Soc.*, 1932, **28**, 101) and $K_2 = 5{\cdot}2 \times 10^{-9}$ (Bray and Connolly, *J. Amer. Chem. Soc.*, 1911, **33**, 1485), we calculate the values shown in Table I. The highest concentration of potassium bromide (0·9M) was chosen such that, for the concentration of bromine used ($0{\cdot}96 \times 10^{-4}$M), the concentration of free bromine was very small and that of hypobromous acid negligible, so that any activity of this solution has to be ascribed solely to the tribromide ion. The variation in the reaction velocity constant ($k_{uni}$) with bromide concentration is given in Table I, and with tribromide-ion concentration in Fig. 2. If the reaction occurs between the phenol molecule and the tribromide ion then, according to Brönsted's theory, the velocity should be proportional to the concentration of this ion, and the linear relationship found between $k_{uni}$ and $[Br_3']$ shows that this is so, the free bromine and bromide ion being without influence except in so far as they determine the concentration of the tribromide ion. From the slope of the line the bimolecular velocity constant for the latter, $k_{bi}^{Br_3'}$, was calculated to be $1{\cdot}4 \times 10^4$ l./g.-mol.-min.

FIG. 2.




If now for the reaction on bromine-water alone it be assumed that only the tribromide ion and hypobromous acid are active, *i.e.*, $k_{uni} = k_{bi}^{Br_3'}[Br_3'] + k_{bi}^{HOBr}[HOBr]$, then $k_{bi}^{HOBr}$ can be determined, and hence the activity of the two brominating agents compared. From Table I we have

$$0{\cdot}023 = 1{\cdot}4 \times 10^4 \times 1{\cdot}068 \times 10^{-8} + k_{bi}^{HOBr} \times 6{\cdot}82 \times 10^{-6}$$

TABLE I.

Total bromine = $c_1$ = 0·96 × $10^{-4}$M; total KBr = $c_2$; temp. = 22·0°.

| $c_2$. | [Br′$_3$]. | [Br′]. | [Br$_2$]. | [HBrO]. | $k_{uni}$, min.$^{-1}$. |
|---|---|---|---|---|---|
| 0 | 1·068 × $10^{-6}$ | 6·797 × $10^{-6}$ | 0·892 × $10^{-4}$ | 6·82 × $10^{-6}$ | *ca.* 0·023 |
| 2·5 × $10^{-3}$ | 0·045 × $10^{-4}$ | 2·5 × $10^{-3}$ (nearly) | 0·91 × $10^{-4}$ | 1·9 × $10^{-8}$ | 0·174 |
| 1·0 × $10^{-2}$ | 0·15 × $10^{-4}$ | 0·01 ,, | 0·66 × $10^{-4}$ | 3·4 × $10^{-9}$ | 0·21 |
| 5·0 × $10^{-2}$ | 0·46 × $10^{-4}$ | 0·05 ,, | 0·50 × $10^{-4}$ | 5·2 × $10^{-10}$ | 0·64 |
| 0·25 | 0·78 × $10^{-4}$ | 0·25 ,, | 0·18 × $10^{-4}$ | 3·7 × $10^{-11}$ | 0·97 |
| 0·9 | 0·92 × $10^{-4}$ | 0·90 ,, | 0·04 × $10^{-4}$ | 2·3 × $10^{-12}$ | *ca.* 1·46 |

which gives $k_{bi}^{HOBr}$ = 0·34 × $10^4$ l./g.-mol.-min., so that on this view the tribromide ion is some four times as effective as the hypobromous acid molecule.

This conclusion is capable of experimental verification, since by using pure hypobromous acid solution it should be possible to work out an independent value of $k_{bi}^{HOBr}$. On a substrate of 1·42 × $10^{-4}$M-hypobromous acid in N/100-sulphuric acid at 22·0°, two velocity measurements gave $k_{uni}$ as 0·75 and 0·77 min.$^{-1}$ (mean, 0·76 min.$^{-1}$), whence $k_{bi}^{HOBr}$ = 0·53 × $10^4$, as compared with the above value of 0·34 × $10^4$ l./g.-mol.-min. Considering the experimental difficulties and the approximations involved, the agreement is satisfactory, and we are led to conclude that the active agents in free bromine-water are the tribromide ion and the hypobromous acid molecule.

Francis' objections against hypobromous acid (see p. 729) have now to be considered in the light of the above conclusions. His bulk bromination experiments were repeated, bromine-water, hypobromous acid, and bromine-water saturated with potassium bromide being used. The concentration of the bromine water (*ca.* $10^{-2}$M) was such that, when it was saturated with potassium bromide (*ca.* 3·5M), the bromine existed practically entirely as the tribromide ion. In this connexion it is of interest that the original reddish-orange colour of the bromine-water changes to a clear yellow on saturation with the bromide. The hypobromous acid solution was prepared as indicated above from the same solution of bromine-water, so its concentration would also be about $10^{-2}$M.

Aniline, as the sulphate, hydrochloride, or free base, gave with bromine-water a white colloidal precipitate which slowly settled out. A precisely similar behaviour was found with the potassium tribromide solution, whereas the hypobromous acid gave coloured colloidal precipitates, as noted by Francis (*loc. cit.*). The hydrochloride and sulphate gave a purple colour and a greenish-blue precipitate, the free base a deep brown colour and a greyish-brown precipitate. With phenol, all three solutions appeared to have an identical effect, *viz.*, formation of a small white precipitate on standing, but with the gold leaf a very marked difference was noted, the rate of attack being followed by means of the " purple of Cassius " test with stannous chloride. Bromine-water alone gave a positive, but very faint reaction after 10 minutes; with hypobromous acid after a similar interval the test was negative, but with the potassium tribromide solution the gold leaf could actually be seen to dissolve, giving an immediate positive reaction with the stannous chloride.

The last objection raised by Francis, concerning the formation, in salt solutions, of mixed halogen addition products, can be overcome by assuming the formation of mixed ions such as [$Br_2Cl$]′ which are active for halogenation. Such ions have been shown to exist in solution by Winkler (J., 1907, **91**, 996; 1908, **93**, 1611). Further evidence was given by a comparison of the properties of the above solution of bromine-water saturated with potassium chloride or bromide, since the colour and the reactivity with aniline and gold leaf appeared to be the same in both cases. Using ethylene, bromine, and a saturated solution of sodium chloride (*ca.* 4·5M), Francis obtained about 45% of α-chloro-β-bromoethane, the remainder being ethylene dibromide. If it be assumed that addition occurs solely through the intermediary of the $Br_2Cl'$ ions, that the addition complex involves one such ion per double bond, and that the probability of the loss of a bromide or a chloride ion from this complex is the same, then the product should contain 50% $C_2H_4ClBr$, 50% $C_2H_4Br_2$, and no $C_2H_4Cl_2$, which is in agreement with experiment. The other mixed addition products found by Francis can be similarly accounted for, and also the observations of Terry and Eichelberger (*J. Amer. Chem. Soc.*, 1925, **47**, 1067), who showed that with sodium maleate and fumarate bromohydrin formation could be prevented by a high concentration of sodium bromide, and that bromine, potassium chloride, and sodium maleate gave the chlorobromo- but no dichloro-compound.

The evidence which has been put forward therefore indicates that, for aqueous bromination at any rate, the activity is due solely to the negative tribromide ion and the hypobromous

acid molecule. Whether in all aqueous halogenations a similar explanation is tenable, is discussed below.

A few experiments with the long-chain phenol using iodine as the substituting agent showed that iodination was extremely slow, on a substrate of $0{\cdot}85 \times 10^{-4}$M-iodine in N/100-sulphuric acid only about 15% having reacted in 2 hours. This slight activity would appear to be mainly due to the hypoiodous acid molecule, as the velocity on a substrate of 0·1M-iodine in 0·5M-potassium iodide, where the iodine exists largely as $I_3'$, was even slower. This agrees with the conclusions of Cofman (*loc. cit.*) and of Soper and Smith (*loc. cit.*), that for the bulk iodination of phenols the activity is due solely to the hypoiodous acid molecule. From the kinetics of the addition of aqueous iodine to β-phenylpropiolic acid, Moelwyn-Hughes and Legard (J., **1933**, 424) have shown that both the tri-iodide ion and the hypoiodous acid molecule are effective in bringing about reaction, the latter being by some 1000 times the more active.

Now, since it has been shown that hypoiodous acid is very much more active than the tri-iodide ion, whereas hypobromous acid and the tribromide ion are of approximately the same order, it would be anticipated that the activity of hypochlorous acid would be very much less than that of the trichloride ion (if, indeed, this exists; see Sidgwick, *Ann. Reports*, **1933**, **30**, 127). As a preliminary, bulk chlorination experiments were carried out on the lines of those previously described with bromine. Chlorine-water (*ca.* 0·01M), a similar solution saturated with potassium chloride (*ca.* 3·5M), and hypochlorous acid (also *ca.* 0·01M) were compared in their reactions with aniline, phenol, anisole, and gold leaf. With phenol, none of the above solutions gave a precipitate; with anisole, hypochlorous acid appeared to have little effect, whereas the other two gave white colloidal solutions, although this experiment was inconclusive owing to the insolubility of the anisole. Aniline (as free base or sulphate) gave with hypochlorous acid almost black colloidal precipitates, whereas the other two solutions gave light brown colloidal solutions, the difference being very marked.

The most striking difference, however, was found with the gold leaf experiments, the solution of which was followed by the "purple of Cassius" test as before. With free chlorine water there was no apparent solution and no positive reaction after 8 minutes, hypochlorous acid behaved similarly after an interval of 30 minutes, but with the chlorine-saturated potassium chloride solution all the gold had disappeared in less than a minute and a positive reaction was shown immediately. A blank experiment using saturated potassium chloride solution alone gave a negative test after 24 hours. These bulk experiments indicated that the trichloride ion existed and that it was an extremely active halogenating agent, and the velocity measurements fully substantiated this.

With the same long-chain phenol at the same surface pressure (2 dynes/cm.) as in the bromination experiments, the variation in the velocity with potassium chloride concentration was studied. The effect was just as pronounced as that of potassium bromide in the bromination, the half-life of the reaction on a substrate of $1{\cdot}15 \times 10^{-4}$M-chlorine in N/100-sulphuric acid decreasing from about 20 minutes (no chloride added) to about 25 seconds in the presence of 2·67M-potassium chloride. The experimental velocities are shown in Table II.

TABLE II.

Substrate, $1{\cdot}15 \times 10^{-4}$M-$Cl_2$ in N/100-$H_2SO_4$. Temp. = 20·0°.

| | | | | | | |
|---|---|---|---|---|---|---|
| Concn. of KCl, M | 0 | 0·01 | 0·04 | 0·20 | 1·5 | 2·67 |
| $k_{uni}$ (min.$^{-1}$) | *ca.* 0·034 | 0·066 | 0·245 | 0·83 | 1·42 | 1·64 |
| $K = [Cl_2][Cl']/[Cl_3']$ (calc.) | | 0·240 | 0·231 | 0·197 | 0·237 | — |

Assuming that at the highest concentration of potassium chloride used all the chlorine existed as trichloride ions, we find that $k_{bi}^{Cl_3'} = 1{\cdot}43 \times 10^4$ l./g.-mol.-min. It is now possible to calculate the equilibrium constant for the reaction $Cl_2 + Cl' \rightleftharpoons Cl_3'$ from the velocity measurements at lower concentrations by ascribing all the activity to the trichloride ion. The results are given in Table II, and indicate a reasonable value of about 0·23 for this constant, since the corresponding values for bromine and iodine are $5{\cdot}7 \times 10^{-2}$ and $1{\cdot}4 \times 10^{-3}$ respectively. The work of Sherrill and Izard (*J. Amer. Chem. Soc.*, **1931**, **53**, 1667) appears to be the only previous attempt to measure this equilibrium constant, their results on the comparison of the solubilities of chlorine and oxygen in aqueous solutions of chlorides giving a value of about 5·8.

The activities of the trichloride ion and the hypochlorous acid molecule were compared after determining that of a pure solution of the latter. Owing to its much slower reaction a

much more concentrated solution than with hypobromous acid had to be used. The unimolecular velocity constant on a substrate of $9{\cdot}23 \times 10^{-3}$M-hypochlorous acid in N/100-sulphuric acid at 20·0° was 0·181 min.$^{-1}$, giving $k_{bi}^{HOCl} = 19{\cdot}6$ l./g.-mol.-min., so that the hypochlorous acid molecule is about $10^3$ times less active than the trichloride ion, as previously anticipated.

These experiments indicate that for substitution reactions involving aqueous halogens both the hypohalous acid and the trihalide ion are the active intermediaries, the activity of the hypohalous acid increasing, and that of the trihalide ion decreasing, with increasing atomic weight of the halogen. The activities thus run inversely as their chemical stability.

Although the above conclusions have direct reference only to substitution reactions, they may well prove to be helpful principles in the study of addition reactions also.

Acknowledgment is made to the Ramsay Memorial Fellowship Trust for a Fellowship and to Professor E. K. Rideal for his valuable advice and criticism.

THE DEPARTMENT OF COLLOID SCIENCE, CAMBRIDGE. [*Received, March 18th*, 1938.]

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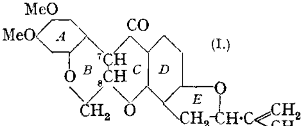
## 137. *The Methylation and Ease of Ring-fission of Rotenone and Related Substances.*

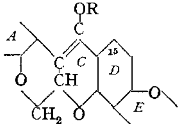
By R. S. CAHN, R. F. PHIPERS, and J. J. BOAM.

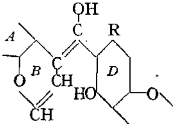
Rotenone, deguelin, and similar substances give methyl ethers derived from the enolic form (II). In similar circumstances toxicarol and dihydrotoxicarol, which contain a phenolic hydroxyl group, give ethers derived from the " open " form (III). This difference shows the greater ease of fission of ring *C* induced by the phenolic hydroxyl group in ring *D* and confirms the views expressed previously.

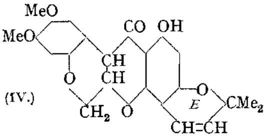
The two types of ether differ markedly in stability to acids, alkalis, and oxidising agents, and in absorption spectra.

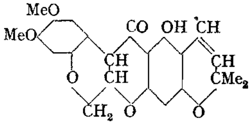
WE showed recently (this vol., p. 513) that very mild alkaline reagents racemise C7 and C8 of rotenone (I) and related substances. We concluded that this occurs by enolisation to (II; R = H), followed by fission of ring *C* to give the " open " form (III; R = H). In the case of toxicarol (IV), racemisation is accompanied by formation of its isomeride, β-toxicarol (V); this structural change, which is reversible, was shown to demand formation of (III; R = OH) as an intermediate, and, since the conditions for the


(I.)


(II.)


(III.)


(IV.)

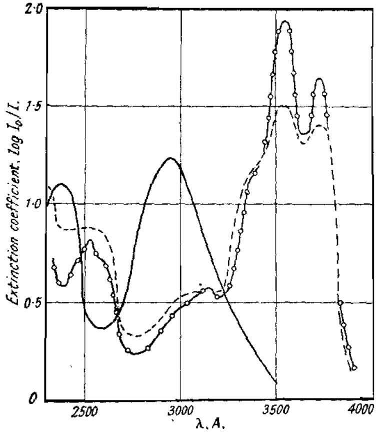

(V.)

structural change and for racemisation are identical, affords strong evidence for the, at least transitory, existence of (III; R = H) during racemisation also of rotenone and its non-phenolic derivatives. We produced evidence that enolisation of toxicarol by alkali is more facile than that of rotenone, and, since we postulated that enolisation is a necessary preliminary to and a causative agent of fission of ring *C*, it followed that this fission to (III) should occur more readily with substances containing a hydroxyl group in ring *D* than

with substances not containing such a substituent. We now present experimental evidence that this is the case. A somewhat similar conclusion had been drawn by Butenandt and Hilgetag (*Annalen*, 1933, **506**, 158), but their evidence was open to the objection raised by us previously (*loc. cit.*) to their other arguments, and their ideas had not in fact found acceptance by other workers.

We have found that substances of the rotenone and toxicarol series are methylated by methyl sulphate in boiling acetone in the presence of aqueous potassium hydroxide or anhydrous potassium carbonate. For the latter method, the acetone must contain about 1% of water, the reaction failing in presence of only 0·5% or of 2% or more of water. The only reference we have found to methylation of these substances (apart from that of their 7-hydroxy-derivatives) is a statement by Clark (*J. Amer. Chem. Soc.*, 1932, **54**, 2537) that toxicarol cannot be methylated by any method. The conditions used by us are such as

FIG. 1.




*Absorption spectra (alcoholic solutions)*:
——— *Rotenone*, 0·00302%, 1 cm.
- - - - - *Acetylrotenone*, 0·00222%, 1 cm.
o——o *Mutarotenone methyl ether*, 0·00217%, 1 cm.

cause racemisation in the absence of methyl sulphate, and the ethers are thus racemic compounds. iso*Rotenone methyl ether*, for instance, is obtained equally well from *l*- and *dl-iso*rotenone and gives *dl-iso*rotenone on acid hydrolysis; acid hydrolysis has been shown (*loc. cit.*) not to cause racemisation. Treatment of rotenone with alkali does not affect the third asymmetric atom, C20, but racemises C7 and C8, thus affording mutarotenone, a semi-racemic, 1 : 1 molecular compound of ordinary *l*-rotenone and *d-epi*rotenone; C20 is lævorotatory in rotenone and *d-epi*rotenone, but C7—C8, considered together, are dextrorotatory in *d-epi*rotenone and lævorotatory in rotenone. The *methyl* ether obtained from rotenone is a similar molecular compound, for it is formed in equal yield from rotenone or mutarotenone and gives mutarotenone on acid hydrolysis.

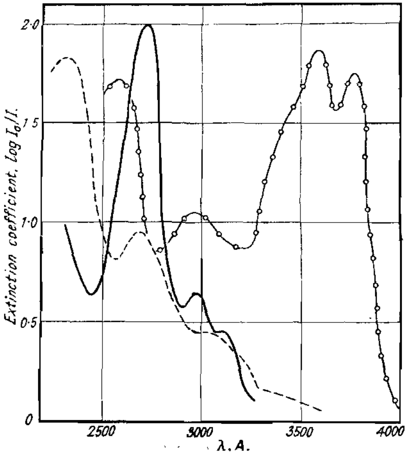
The ethers from rotenone and *iso*rotenone are derivatives (II; R = Me) of the enolic form, analogous to the known acetates (II; R = Ac). The possibility that they are derived by methylation of the phenolic hydroxyl group in ring *D* of the " open " form (III) is excluded by their very ready hydrolysis by dilute acid. Further, as shown in Fig. 1,

the absorption spectrum of rotenone methyl ether has the characteristic maximum of acetylrotenone (with its two well-defined bands and a third less definite band constituting a triplet) and differs radically from that of rotenone. These ethers are unaffected by iodine or by air in alkaline solution, reagents which rapidly attack the CH·CO of rotenone derivatives. They are also remarkably stable to alkali* and are indeed best purified by destroying unmethylated material and accompanying by-products by hot alcoholic alkali hydroxide.

Similar acid-labile enolic *ethers* are obtained from deguelin (VI) and dihydrodeguelin.

Methylation of toxicarol gives, as anticipated, a *dimethyl* ether by both methods. However, in contrast to the ethers discussed above, this substance is stable even to 10% mineral acid, whereas 2% acid suffices to hydrolyse the enolic ethers. In further contrast,

FIG. 2.



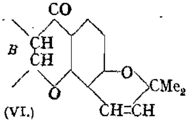

*Absorption spectra (alcoholic solutions)*:

——— *Toxicarol*, 0·00234%, 1 cm.
- - - - - - *Toxicarol dimethyl ether*, 0·00206%, 1 cm.
o———o *Diacetyltoxicarol*, 0·00335%, 1 cm.

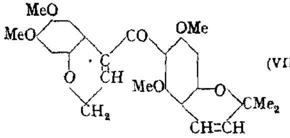
it is very readily resinified by alkali and absorbs oxygen rapidly in the presence of dilute alkali. These properties find a natural explanation if the ether is the αβ-unsaturated ketone (VII), derived from the "open" form (III; R = OH), and this structure is in agreement with the absorption spectrum. As shown in Fig. 2, the absorption of diacetyltoxicarol, which has the structure (II; R = Ac) but with the second acetoxy-group attached to C15, closely resembles that of acetylrotenone and rotenone methyl ether, but the absorption of toxicarol dimethyl ether differs from that of toxicarol and the diacetate. The structure (VII) is further in line with formation of the ether in equal yield from α- and from β-toxicarol, as also with the results of hydrogenation.

* On account of the stability to air and alkali it was possible that the ethers might have advantages as insecticides, but experiments by Mr. Craufurd-Benson of this Organisation showed that they have relatively little toxicity compared with their unmethylated prototypes.

Hydrogenation of the dimethyl ether gives smoothly a *tetrahydro*-ether, in which all the methoxyl groups are retained and which we believe to be (VIII). Dihydro-α-toxicarol



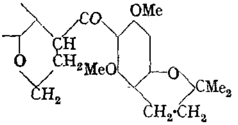
(VI.)

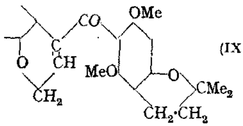


(VII.)

[as (IV), but with the ethylenic linking in ring *E* reduced] gives a *dimethyl* ether, which is stable to acid and is thus believed to be (IX); on hydrogenation this yields the same tetrahydro-ether (VIII) as is obtained from toxicarol dimethyl ether.

(VIII.)





(IX.)

We did not investigate reduction of mutarotenone methyl ether owing to the possibilities for isomerism, but used instead deguelin methyl ether. The product appeared to have lost a methyl group, which was not unexpected behaviour for an enolic ether, but the analytical figures for carbon and hydrogen were unintelligible, and, with only a small amount of material available, we were unable to establish the course of this reaction.

It is noteworthy that the yield of toxicarol dimethyl ether is 50%, whereas that of the enolic ethers is at most 30%. With the latter is obtained much gum, which is not unreacted starting material, and we think it at least possible that these gums contain the "open" phenolic ethers derived from (III; R = H).

Rotenone, *iso*rotenone, deguelin, and dihydrodeguelin differ only in the nature of ring *E* and give enolic ethers of type (II). Toxicarol and dihydrotoxicarol have in ring *E* the structure of deguelin and dihydrodeguelin, respectively, but give "open" ethers. It is thus clearly the original phenolic hydroxyl group in ring *D* which causes the relatively easier fission of its neighbouring ring *C* in the toxicarol series. We regard this proof and the incidental isolation of actual derivatives of the "open" form as the final steps in the series of arguments developed in our earlier publication.

In the preparation of dihydrotoxicarol dimethyl ether we isolated also a small amount of a *monomethyl* ether. Toxicarol gives a similar by-product, but the properties of this *substance* (cf. p. 740) leave us in doubt whether it is really the monomethyl ether.

## EXPERIMENTAL.

Methoxyl determinations were carried out as described previously. The [α] values are only approximate, as no accurate polarimeter was available; temperatures and concentrations are therefore omitted, but the latter were usually 5—6% in this and our previous work.

*Mutarotenone Methyl Ether.*—(*a*) Rotenone (2 g.), methyl sulphate (2 c.c.), and potassium carbonate (5 g.) in acetone (20 c.c.) were heated under reflux for 1—2 hours, the mixture then poured into water, and the gummy product crystallised from alcohol (the use of too little alcohol led to separation of oils). The m. p. of the product thus obtained varied, but a rather large number of crystallisations was always needed for purification. However, if the crude crystalline product was heated in 20 parts of 2% alcoholic potassium hydroxide for 15 minutes under reflux and the mixture was then cooled, acidified with acetic acid, and, if necessary, concentrated until crystallisation occurred, one to three further crystallisations usually sufficed. The crude, oily product gave discoloured gums when heated with alkali, as would be expected if "open" ethers were present. Varying the time of heating the original mixture beyond the limits stated gave reduced yields. The yield of pure product from the above batch was usually

about 30%, but it was often less from larger batches. In experiments starting with dried acetone, we recovered unchanged rotenone when the acetone contained 0, 0·25, or 0·5% of water, and got mutarotenone when the acetone contained 2% of water.

Pure *mutarotenone methyl ether* forms needles, m. p. 141°, $[\alpha]_D$ −130° in benzene [Found C, 70·5, 70·8; H, 6·2, 6·1; OMe, 23·0. $C_{21}H_{15}O_3(OMe)_3$ requires C, 70·55; H, 5·9; OMe, 22·8%]. The m. p. is unreliable as a criterion of purity (cf. the analogous molecular compound, mutarotenone), being little influenced by the presence of impurities, but depressions of 5° or more are obtained after about equal amounts of the ether and mutarotenone have been mixed on a porous tile. One specimen having approximately the correct m. p. was shown by its absorption spectrum to contain 30% of rotenone. The ether is insoluble in alkali, gives no colour with ferric chloride and none in the Goodhue test; it gives a blue colour in the Durham test. It is more soluble in the usual organic solvents than is rotenone or mutarotenone, and this is responsible for the difficulty in purifying it by crystallisation. It gives no oxime under the conditions used for rotenone. It absorbs no oxygen when stirred in 1% alcoholic sodium hydroxide solution under air and is unaffected by iodine and sodium acetate in hot alcohol or by heating under reflux for 1 hour in 5% alcoholic potassium hydroxide solution with or without the addition of 20% of water.

(*b*) The same ether was obtained in the same yield from mutarotenone by the above method.

(*c*) Potassium hydroxide (2 g.) in water (30 c.c.) was added to a hot solution of rotenone (4 g.) and methyl sulphate (4 c.c.) in acetone (100 c.c.), and heating was continued for 10 minutes. The resultant red solution was poured into water, made feebly acid, and kept overnight. The supernatant liquid was then decanted from the gummy product, which by several crystallisations from alcohol gave the ether (0·2 g.), m. p. 141—142°.

(*d*) Attempted methylation by method (*a*), but using methyl *p*-toluenesulphonate in place of methyl sulphate (cf. p. 740), gave mutarotenone.

*Hydrolysis of Mutarotenone Methyl Ether.*—The ether (1 g.) was heated under reflux in alcohol (18 c.c.) containing concentrated sulphuric acid (2 c.c.). The product (0·7 g.), isolated after 60 minutes by pouring into water, crystallised from alcohol in clusters of small needles, $[\alpha]_D$ −80° in benzene, m. p. 146°, raised by further crystallisation to 148° (alone or mixed with an authentic sample). Hydrolysis was actually complete after 15 minutes' heating, as was shown by working up a small portion of the reaction mixture. Identity was confirmed by dissolving the product (0·5 g.) in carbon tetrachloride (5 c.c.), from which rotenone–carbon tetrachloride solvate (0·25 g.; identified in the usual way by conversion into rotenone, etc.) separated; the gum obtained from the carbon tetrachloride mother-liquors deposited 0·1 g. of mutarotenone from ether, but no further crystalline material was obtained. This behaviour is typical of mutarotenone. Taken in conjunction with the mixed m. p. and the rotation, it leaves no doubt as to identity.

Mutarotenone (0·6 g.) was similarly obtained when the ether (1 g.) was heated with alcohol (20 c.c.) containing concentrated sulphuric acid (0·4 c.c.). When, however, only 0·1 c.c. of sulphuric acid was used, the product tended to separate from alcohol as an oil, indicating incomplete hydrolysis; only unchanged ether (0·1 g.), m. p. 137—140° (mixed m. p.), was obtained crystalline. When the ether (0·5 g.) was heated under reflux for ½ hour in alcohol (7·5 c.c.) containing sulphuric acid (2·5 c.c.), isomerisation accompanied hydrolysis, and the product was *dl-iso*rotenone (0·1 g.), m. p. 161—163°, raised to 163—166° by mixing with an authentic specimen and depressed to 150—153° by mixing with rotenone.

dl-iso*Rotenone Methyl Ether.*—*dl-iso*Rotenone (5 g.), potassium carbonate (12·5 g.), and methyl sulphate (5 c.c.) in acetone (50 c.c.) were heated under reflux for 4 hours (better than 2 hours in this case). The oily product, isolated by pouring the mixture into water and decanting the supernatant liquid, was dissolved in hot alcohol. Crystals (1·5 g.), m. p. 165—175°, separated. When these were dissolved in hot alcohol and the crystals which separated within 1—2 hours were collected, pure dl-iso*rotenone methyl ether* (0·6 g.) was obtained as colourless plates, m. p. 189—190° [Found: C, 70·4; H, 5·7; OMe, 21·7 (micro; Weiler), 23·2 (Boam). $C_{21}H_{15}O_3(OMe)_3$ requires C, 70·55; H, 5·9; OMe, 22·8%], the m. p. being unchanged by further crystallisation. Concentration of the mother-liquor and collection of the crystals which separated again within 1—2 hours gave a further 0·5 g. of the ether, m. p. 188—190°. If, however, the alcoholic solutions were kept for longer times before collection of the crystals, the yield was higher but the material usually began to melt at about 165° and probably contained *iso*rotenone, since it gave the Goodhue test, which is not given by the pure ether. The crude crystalline product may also be purified by hot 2% alcoholic potassium hydroxide, as detailed for mutarotenone methyl ether; the technique of crystallisation just described then becomes unnecessary.

Purification of *iso*rotenone methyl ether is in any case not difficult, as the ether is the least soluble component of the reaction product.

*l-iso*Rotenone, when treated similarly, gave a similar yield of the same ether (mixed m. p.; α 0°), which required the same technique for purification. It was entirely racemised during the reaction, for the crude product, m. p. 165—175°, had α 0° in benzene.

Hydrolysis of the ether by dilute acid, as described for mutarotenone methyl ether, gave *dl-iso*rotenone

*Methyl Ethers of Deguelin and Dihydrodeguelin.*—A mixture of deguelin (1 g.), potassium carbonate (2 g.), methyl sulphate (1 c.c.), and acetone (10 c.c.) was boiled under reflux for 2 hours and then poured into water. Trituration of the gummy product with alcohol gave *deguelin methyl ether* (0·4 g.), m. p. 143—148°. Recrystallisation from alcohol yielded needles, m. p. 149—150° [Found: OMe, 24·4. $C_{21}H_{15}O_3(OMe)_3$ requires OMe, 22·8%].

When this ether (0·2 g.) had been boiled for ½ hour in alcohol (10 c.c.) containing sulphuric acid (0·5 c.c.), the solution, after cooling, deposited deguelin (0·1 g.), which after recrystallisation from alcohol had m. p. 170° alone or mixed with an authentic specimen.

Dihydrodeguelin (1 g.), when heated with potassium carbonate (2 g.) and methyl sulphate (2 c.c.) in acetone (40 c.c.) for 5 hours, gave a crude *methyl* ether (0·7 g.), m. p. 147°, which was obtained as stout, colourless needles, m. p. 152—154°, after two crystallisations from alcohol (Found: C, 70·5; H, 6·0. $C_{24}H_{26}O_6$ requires C, 70·3; H, 6·3%).

It is remarkable that dihydrodeguelin, in contrast to deguelin, does not give the Goodhue test.

*Hydrogenation of Deguelin Methyl Ether.*—The ether (1 g.) in a previously reduced mixture of Adams's platinum catalyst (about 0·05 g.) and acetic acid (50 c.c.) absorbed 154 c.c. (N.T.P.) of hydrogen (1 mol. = 54 c.c.). Dilution of the filtered solution with water and two crystallisations of the precipitate (0·75 g.) from alcohol gave pale yellow leaflets, m. p. 155—157° (Found: C, 69·3; H, 5·55; OMe, 15·9%). A substance with three methoxyl groups requires 22% or more of OMe. The product is probably not dihydrodeguelin (Calc. for $C_{23}H_{24}O_6$: C, 69·7; H, 6·1%), and is definitely not dihydrodeoxydeguelin (Calc. for $C_{23}H_{26}O_5$: C, 72·2; H, 6·8%).

*Methylation of Toxicarol.*—(*a*) Toxicarol (20 g.), anhydrous potassium carbonate (40 g.), and methyl sulphate (20 c.c.) in acetone (400 c.c.) were heated under reflux for 2 hours. The gummy product, obtained by pouring the mixture into water, crystallised readily when triturated with hot alcohol. The *dimethyl* ether (VII) (10 g.) was collected from the cooled solution as greenish-yellow, red, or even purple needles, m. p. 168—169°. In spite of the colour, it was nearly pure, for the pure ether, which is pale yellow, melts at 169—170° (Found: C, 68·5; H, 6·05. $C_{25}H_{26}O_7$ requires C, 68·4; H, 6·0%). The colour varied greatly in different preparations, but appeared to be definitely less intense or even absent if the aqueous mixture was acidified before the gummy product settled to the bottom of the vessel. The red colour, often very tenaciously retained, has been removed by boiling the product in alcohol with a fairly large amount of charcoal for 2 hours and, in another experiment, by passing the ether in chloroform through a short column of activated alumina; on the other hand, on another occasion the colour was deepened by boiling the ether with charcoal in alcohol. The ether gives no colour with ferric chloride and is unchanged by acetylation. In the Goodhue test it gives a blue colour with a mnch more pronounced red tinge than is usual. The ether, even when pure, is rapidly resinified by hot alcoholic sodium hydroxide, addition of even one drop of alkali causing appearance of a brown colour within 30 seconds. The red impurity leads to the production of blue or green colours by traces of mineral acid, but the yellow ether has been recovered unchanged after heating on the water-bath for 1 hour with 20% alcoholic sulphuric acid. The ether in 1% alcoholic sodium hydroxide absorbs oxygen very rapidly when stirred under air; it absorbs iodine under the conditions used for dehydrogenation. It gives only a faint brown colour in the Durham reaction.

(*b*) By the above method β-toxicarol (1 g.) gave needles (0·3 g.), m. p. 167—168°, which resembled the above ether in every way and did not depress its m. p.

(*c*) Potassium hydroxide (6 g.) in water (100 c.c.) was added to a boiling solution of toxicarol (20 g.) and methyl sulphate (10 c.c.) in acetone (1200 c.c.); the mixture was then evaporated to about 250 c.c. during 30 minutes and poured into water. The red gum precipitated was repeatedly crystallised from alcohol containing a little benzene and thus gave the dimethyl ether (9 g.) as pink, stout prisms from a dilute, or needles from a concentrated, solution; they had m. p. 168—170° alone or mixed with the ether prepared by method (*a*) [Found: OMe, 28·3, 29·1. $C_{21}H_{14}O_3(OMe)_4$ requires OMe, 28·3%]. Concentration of the mother-liquors and finally evaporation at room temperature gave a *substance*, which after repeated crystallisation

from alcohol–benzene formed pale yellow rhombs, m. p. 190—192°. From analyses (Found: C, 67·8, 67·6; H, 5·7, 5·6; OMe, 22·0, 21·5%), we thought this to be toxicarol monomethyl ether [Calc. for $C_{21}H_{15}O_4(OMe)_3$: C, 67·9; H, 5·7; OMe, 21·4%] but it appears to be identical with the product described in the following paragraph, where its nature is discussed.

(*d*) Toxicarol (10 g.), methyl *p*-toluenesulphonate (6 g.), and potassium carbonate (20 g.) in acetone (200 c.c.) were heated under reflux for 3 hours. The product was isolated in the usual way as pale yellow crystals (3·8 g.), m. p. 171—180°, from alcohol. Two crystallisations from alcohol, during which a small amount of less soluble, high-melting material was allowed to remain undissolved and removed, gave a product, m. p. 181—184°, also giving fairly correct analytical results for toxicarol monomethyl ether (Found: C, 67·45; H, 5·65%). The m. p. was not raised above 182—184° by crystallisation from alcohol or acetic acid, but the substance melted at about 186° when mixed with the product, m. p. 190—192°, described in (*c*). Diagnosis as the monomethyl ether appeared confirmed by further methylation of the substance by method (*a*) to give very pure dimethyl ether in 70% yield. The preparation was repeated several times with modification of the method of isolating the product in attempts to explain the divergence in melting points and the fact that a green colour developed within 15—60 seconds, but not instantaneously, when a drop of ferric chloride solution was added to the substance in alcohol. In one experiment no methylation occurred and we isolated only α- and β-toxicarol (this was, in point of time, the first occasion on which we obtained β-toxicarol); in some experiments we obtained unworkable gums, but in yet others we were able to obtain the substance, m. p. about 182°, without difficulty. From one sample, m. p. 182°, we isolated α-toxicarol by means of alkali but were unable to identify the non-phenolic portion. From another sample we obtained dihydro-β-toxicarol by hydrogenation. In the Durham reaction the substance gives the blue colour given by β-toxicarol and by dihydro-α-toxicarol monomethyl ether. We thus leave the nature and indeed the homogeneity of these substances, m. p. 182—184° and 190—192°, in doubt.

(*e*) Attempts to methylate toxicarol by the Schotten–Baumann method with or without the addition of ether, by pyridine and methyl sulphate in the cold (30 minutes), and by diazomethane failed.

*Methylation of Dihydro-α-toxicarol.*—Dihydro-α-toxicarol (2 g.), anhydrous potassium carbonate (4 g.), and methyl sulphate (2 c.c.) in acetone (20 c.c.) were heated under reflux for 5 hours. The mixture was diluted with water and shaken with ether. The ethereal layer was washed successively with aqueous potassium hydroxide, dilute hydrochloric acid, and water, dried, and evaporated. Slow crystallisation of the residue from alcohol gave a mixture of feathery needles and large prisms, which were separated by hand-picking. Repeated crystallisation of the needles from alcohol, in which they were sparingly soluble, gave colourless needles, m. p. 202°; these give no colour with ferric chloride and are thus the true *monomethyl* ether of dihydro-α-toxicarol (phenolic group methylated without ring-fission) [Found: C, 67·7; H, 6·2; OMe, 21·7. $C_{21}H_{17}O_4(OMe)_3$ requires C, 67·6; H, 6·1; OMe, 21·8%]. Repeated crystallisation of the prisms from alcohol, in which they were more soluble than were the needles, gave the "*dihydro-dimethyl ether*" (IX) as colourless prisms or plates, m. p. 176° [Found: C, 67·5; H, 6·1; OMe, 28·7. $C_{21}H_{16}O_3(OMe)_4$ requires C, 68·2; H, 6·4; OMe, 28·8%]. In the Durham test the monomethyl ether gives a blue colour, the dimethyl ether only a very pale brown.

When the dimethyl ether (IX) (0·2 g.) was boiled under reflux in 5% alcoholic hydrochloric acid (10 c.c.) for ½ hour, the product had a bright, deep green colour. It was, however, completely decolorised by charcoal, and the dimethyl ether (IX) was recovered unchanged.

*The "Tetrahydro-dimethyl Ether" (VIII) of Toxicarol.*—(*a*) The dimethyl ether (VII) (m. p. 169—170°; 2 g.) of toxicarol in glacial acetic acid (50 c.c.) containing a previously reduced Adams's platinum catalyst absorbed 2 mols. of hydrogen. The gummy precipitate obtained by diluting the filtered solution with water, when crystallised from alcohol, gave the "*tetrahydro-dimethyl ether*" (VIII) (1·44 g.) as colourless leaflets, m. p. 175—176° [Found: C, 67·8; H, 6·9; OMe, 29·2. $C_{21}H_{18}O_3(OMe)_4$ requires C, 67·9; H, 6·8; OMe, 28·0%]. These strongly depress the m. p. of the dihydro-ether (IX), which melts at the same temperature.

(*b*) The dihydro-ether (IX) (0·5 g.), hydrogenated in acetic acid (50 c.c.) in the same way, gave the tetrahydro-ether, m. p. 176° alone or mixed with the ether prepared by method (*a*), and depressed by admixture with the starting material.

*Methylation of* Derris *Extract.*—(*a*) A commercial *Derris* extract (10 g.; rotenone content 27%; Goodhue value 48·5; OMe 13·5%), methyl sulphate (10 c.c.), and potassium carbonate (10 g.) in acetone (100 c.c.) were heated under reflux for 2 hours. An excess of powdered ammonium carbonate was gradually introduced and the mixture was kept for 2—3 hours after

the main exothermic reaction had ceased. The whole was then poured into water and extracted with ether. The ethereal layer was exhaustively washed with water, dried, and evaporated. The product had Goodhue value 35 and OMe 16·2%. Repetition of the process gave a product having $[\alpha]_D$ −43·7° in benzene (mol. wt. assumed as that of rotenone), OMe 16·9%, and Goodhue value 28. This [α] was about a half to one-third of that of the original extract; [α] of the extract could not be determined accurately on account of the colour, and treatment with charcoal removed some optically active material. A third methylation gave material with OMe 18·0% and Goodhue value about 15. The product was a reddish resin, resembling pitch in consistency. Removal of every trace of methyl sulphate is essential for stability, and the ammonium carbonate procedure is convenient for this purpose. Rotenone and deguelin were main ingredients of the original extract; thus, methylation is evidenced by the decrease in Goodhue value (cf. Cahn, Phipers, and Boam, *J. Soc. Chem. Ind.*, 1938, in the press) as well as by the increase in methoxyl content.

(*b*) A Sumatra-type extract (rotenone content 4%; ferric chloride value 60; Goodhue value 14; OMe 12·5%) gave similarly a product having OMe 17·4%, ferric chloride value 19·5, and Goodhue value 22. A second treatment gave a product having OMe 21·9%, ferric chloride value 0 (trace of yellow colour only), and Goodhue value 31 (having the violet-red shade characteristic of toxicarol dimethyl ether). Toxicarol was a main ingredient of the original extract, and methylation is evidenced by the decrease in ferric chloride value (cf. *loc. cit.*) and the increase in Goodhue value (due to formation of toxicarol dimethyl ether) as well as by the change in methoxyl content.

*Absorption Spectra.*—We are much indebted to Dr. A. E. Gillam, who, by kind permission of Professor I. M. Heilbron, determined the absorption spectra recorded, using the technique detailed in our earlier paper. Data for rotenone, toxicarol, and the acetyl derivatives are taken from that paper. Maxima and molecular extinction coefficients observed for the ethers in freshly prepared solution in purified alcohol were:

| | λ of max. in A. | Mol. extinction coeff., ε. |
|---|---|---|
| Rotenone methyl ether ......... | 3735 | 31,000 |
| | 3540 | 36,500 |
| | 2530 | 15,200 |
| Toxicarol dimethyl ether ...... | 2310 | 39,000 |
| | 2680 | 20,200 |

We are indebted to Messrs. Cooper, McDougall, and Robertson, Ltd., Berkhamsted, for permission to publish these results.

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## 138. *A Contribution to the Stereochemistry of Anils.*

By V. de Gaouck and R. J. W. Le Fèvre.

The dipole moments now recorded for certain simple Schiff's bases, R·CH:NR′, show that these are compounds in which the groups R and R′ stand in the *trans*-relation about the C═N linking.

The possibility that phototropic changes in this group of compounds involve configurational changes of the *cis* ⇌ *trans* type is diminished by the present work.

The possibility that phototropy (*i.e.*, the reversible change of colour occurring when certain compounds are exposed to light; *Z. physikal. Chem.*, 1899, **30**, 140) involves configurational changes has led us to consider the stereochemistry of anils, because among these are found the best common examples of this phenomenon (*e.g.*, salicylidene-*m*-toluidine; Senier and Shepheard, J., 1909, **95**, 441, and later papers).

The space formulæ of these compounds are not well established. In certain cases, the isolation of two forms has been claimed (cf. Hantzsch and Schwab, *Ber.*, 1901, **34**, 822), but these are of doubtful authenticity and may possibly be due to dimorphism rather than geometrical isomerism (Freudenberg, " Stereochemie," 1933, p. 1097).

In the course of the present work we have examined two of these examples. Anselmino (*Ber.*, 1907, **40**, 3465) has stated that two crystallograph cally different forms of salicyl-

ideneaniline, *d* 1·087 and 1·184 (Jaeger, *ibid.*, p. 3474), are produced by cooling either a hot alcoholic or a ligroin solution. We have therefore prepared two such specimens and made dielectric-constant and density measurements for various solutions of them in benzene. These results are tabulated below, together with the coefficients of increase of dielectric constant and density with concentration ($\alpha\epsilon_2$ and $\beta d_2$ respectively). The identity of these values for both materials shows that in solution only *one* molecular species is present. Therefore, it may be assumed that this alleged case of isomerism is also due to polymorphism.

*Salicylideneaniline* (*M*, 197).

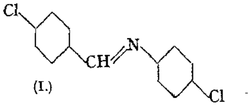
| $w_1$ | $\epsilon^{1900}_{25°}$ | $d^{25°}_{4°}$ | $\alpha\epsilon_2$ | $\beta d_2$ | $n^{25°}_D$ | $r_{12}$ | $[R_L]_D$ |
|---|---|---|---|---|---|---|---|
| 0·0061235 | 2·2954 | 0·87503 | 3·74 | 0·204 | 1·49813 | 0·33035 | 66·6 |
| 0·0076107 | 2·3012 | 0·87535 | 3·77 | 0·206 | 1·49826 | 0·33501 | 65·5 |
| 0·0085037 | 2·3092 | 0·87557 | 4·27 | 0·208 | 1·49839 | 0·33499 | 65·1 |
| 0·0103572 | 2·3117 | 0·87601 | 3·78 | 0·208 | 1·49877 | 0·33504 | 67·9 |
| (The above data refer to a specimen obtained from ligroin, and those below to one obtained by recrystallisation from alcohol.) | | | | | | | |
| 0·0049824 | 2·2910 | 0·87484 | 3·71 | 0·213 | 1·49807 | 0·33507 | 67·1 |
| 0·0073309 | 2·2996 | 0·87529 | 3·70 | 0·206 | 1·49827 | 0·33503 | 66·0 |
| 0·0081481 | 2·3031 | 0·87548 | 3·75 | 0·209 | 1·49834 | 0·33500 | 65·0 |
| 0·0113446 | 2·3156 | 0·87613 | 3·80 | 0·207 | 1·49897 | 0·33511 | 67·4 |

Another apparently clear claim for the discovery of two different forms was made by Brewster and Millam (*J. Amer. Chem. Soc.*, **1933**, **55**, 763) for 5-bromosalicylidene-*o*-toluidine; according to them, varieties of m. p. 165° * or 86·5° were obtained by heating together the aldehyde and the amine respectively with or without addition of alcohol. In several attempts to follow the brief directions, we have always obtained the form of lower m. p.

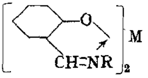
As the common Schiff's bases, therefore, presumably occur in one form only, it became of interest to determine the natures of these forms and whether they are derived from a general configuration. To this end we have prepared, and made dipole-moment measurements on, the compounds named in the following table:

| | *M.* | $\alpha\epsilon_2$. | $\beta d_2$. | $_\infty P_1$. | $[R_L]_D$. | $\mu$, D. |
|---|---|---|---|---|---|---|
| Benzylideneaniline | 181 | 1·85 | 0·170 | 112·6 | 61·6 | 1·57 |
| *p*-Chlorobenzylideneaniline | 215·5 | 1·96 | 0·215 | 134·8 | 69·9 | 1·77 |
| *p*-Chlorobenzylidene-*p*-toluidine | 229·5 | 2·41 | 0·232 | 161·5 | 73·5 | 2·06 |
| *p*-Chlorobenzylidene-*p*-chloroaniline | 250 | 1·37 | 0·291 | 121·3 | 71·0 | 1·56 |
| Salicylideneaniline | 197 | 3·75 | 0·208 | 190·1 | 66·4 | 2·45 |
| Salicylidene-*m*-toluidine | 211 | 3·84 | 0·192 | 208·5 | 70·2 | 2·59 |
| *o*-Methoxybenzylideneaniline | 212 | 5·10 | 0·192 | 259·8 | 71·7 | 3·02 |
| 5-Bromosalicylideneaniline | 263 | 1·52 | 0·331 | 130·9 | 101·5 | 1·19 |

From the essential identity—within the limits of experimental error—of the moments of benzylideneaniline and *p*-chlorobenzylidene-*p*-chloroaniline (I), it is evident that the latter compound must have a *trans*-structure and that, in it, the two C–Cl links must be approximately parallel. Such a conclusion is completely reconcilable, if normal valency angles and




(I.)




(II.)

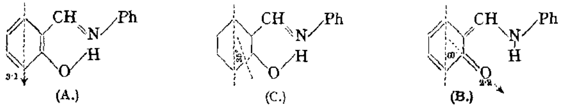
atomic dimensions are assumed, with the values found for *p*-chlorobenzylideneaniline and its 4′-methyl derivative. It is therefore not improbable that throughout the whole series the *trans*-configuration is so much the more stable that it alone occurs.

The analysis of the data for the *o*-hydroxy-compounds is rendered exceedingly difficult by the possibilities of intramolecular rotation. Thus, both the hydroxyl and the CH=NR groups can, by rotation about the links holding them to the benzene nucleus, present various mutual orientations, for which resultant dipole moments varying by as much as 3 D. will be

* This m. p. is very close to that of 5-bromosalicylic acid.

appropriate. In this connexion, however, we may mention that whilst this work was in progress Hunter and Marriott (J., 1937, 2000) described a number of bimolecular metallic derivatives of the salicylidene-anils and formulated them as co-ordination compounds of the type (II). They recognise this as evidence for the *trans*-configuration of those particular anils and further cite the infra-red spectroscopic investigations of Wulf, Hendricks, Hilbert, and Liddel (*J. Amer. Chem. Soc.*, 1936, **58**, 1991) together with supporting solubility and m. p. relationships.

The present measurements are not in discord with this suggestion, for, although admittedly the magnitude of the moment determined experimentally for such a system cannot be estimated with any certainty, yet we note that the observed figure stands *within* the limits which may reasonably be expected for the two chief extreme unreal structures (A) and (B). These we have estimated by assuming that the oxygen, hydrogen, and nitrogen



atoms and the methin and phenyl groups all subtend angles of 120° with their immediate neighbours and that the following link moment values apply: CH═N, 2·5; Ph—N, 1·5; C—O, 0·7; C═O, 2·3; H—O, 1·5; H—N, 1·6 D. On these premises, (A) has a resultant of approximately 3·1 D. acting nearly vertically, and (B) one of 2·2 D. acting roughly parallel to the C═O axis. The apparent direction of the resultant in the real structure (C) may, however, be inferred from the observed moment of 5-bromosalicylideneaniline (1·19 D.), by regarding this value as arising from the interaction of the C–Br vector along the oxygen ⟶ carbon directions in (A) and (B) with the resultant, 2·45, found for salicylideneaniline. The direction of action of the latter is thence found as 35° to the vertical (C), *i.e.*, *between* the values for (A) and (B).

Finally, attention may be directed to the differences in moment between salicylideneaniline and its methyl ether. Since resonance of the type discussed is impossible with the latter, it might be expected to have the larger moment, corresponding to (A), but against this must be offset the effect of the replacement of the greater H→O link moment by the smaller $CH_3$→O value (cf. phenol, $\mu = 1·7$; anisole, $\mu = 1·2$ D.) The actual experimental value is 3·02 D.

Since it seemed possible that light might cause an inversion of configuration, as it does in the similar cases of certain oximes, azo-compounds, etc., we have several times throughout the present work made the solutions in brown glass bottles and rigorously excluded white light until after the dielectric-constant measurements had been completed. Such solutions were then exposed in quartz cells to the direct light of a mercury arc for periods up to 12 hours, transferred as rapidly as possible to the dielectric-constant apparatus, and re-measured. In no case was any significant change observed, a negative result kindly confirmed—for solutions of far lower concentrations than those employed by us—by Dr. G. S. Hartley, of this department, using an electric photometric method.

We conclude, therefore, that the present work diminishes the possibility that phototropic changes among the anils involve configurational inversions of the *cis* ⇌ *trans*-type.

## EXPERIMENTAL.

*Preparation of Materials.—Salicylidene*-m-*toluidine*. The crude solid from a direct condensation, dissolved in ethyl alcohol at room temperature and cooled to − 20°, gave yellow needles, m. p. 39° (cf. Gallagher, *Bull. Soc. chim.*, 1921, **29**, 683).

p-*Chlorobenzylidene-aniline and* -p-*chloroaniline*. The crude materials, washed first with very dilute acetic acid, then with water, and finally crystallised from alcohol, afforded pale yellow plates, m. p. 62°, and yellowish-white needles, m. p. 112°, respectively (Walther and Raetze, *J. pr. Chem.*, 1902, **65**, 265).

p-*Chlorobenzylidene*-p-*toluidine and* 5-*bromosalicylideneaniline*. These were prepared as in

*the previous cases. Both were crystallised from alcohol,* and formed needles, m. p. 126°, and golden needles, m. p. 119°, respectively. 5-Bromosalicylaldehyde was conveniently prepared according to Brewster and Millam (*loc. cit.*).

*Benzylidene- and salicylidene-aniline.* After recrystallisation from alcohol, benzylideneaniline had m. p. 49·5°. Salicylideneaniline was recrystallised from alcohol and from ligroin; this procedure was claimed by Anselmino (*loc. cit.*) to produce two crystallographically different forms, m. p. 50·5°, one appearing as needles from alcohol, the other as rhombs from ligroin.

o-*Methoxybenzylideneaniline.* The product of direct condensation at 100° was cooled to − 70° with ether–solid carbon dioxide. After recrystallisation from alcohol, the substance formed needles, m. p. 44° (cf. Noelting, *Ann. Chim. Phys.*, 1910, **19**, 540).

*Dipole-moment Measurements.*—These were carried out in benzene at 25° and 1200 kc. The apparatus and other details are described elsewhere. The necessary observations are tabulated below and on p. 742 under the following headings: $w_1$, the weight-fraction of the solute in the solutions; $\varepsilon_{25^\circ}^{1200}$ and $d_{4^\circ}^{25^\circ}$, the dielectric constants and densities of the solutions at the above

| $w_1$. | $\epsilon_{25^\circ}^{1200}$. | $d_{4^\circ}^{25^\circ}$. | $\alpha\epsilon_2$. | $\beta d_2$. | $n_D^{25^\circ}$. | $r_{12}$. | $[R_L]_D$. |
|---|---|---|---|---|---|---|---|
| 0 | 2·2725 | 0·87378 | — | — | 1·49724 | 0·33503 | — |
| *Benzylideneaniline* (*M*, 181). | | | | | | | |
| 0·0052333 | 2·2822 | 0·87468 | 1·85 | 0·172 | 1·49786 | 0·33504 | 61·0 |
| 0·0069171 | 2·2859 | 0·87497 | 1·94 | 0·172 | 1·49811 | 0·33507 | 61·6 |
| 0·0071341 | 2·2853 | 0·87499 | 1·79 | 0·170 | 1·49813 | 0·33506 | 61·4 |
| 0·0101883 | 2·2912 | 0·87548 | 1·83 | 0·170 | 1·49857 | 0·33513 | 62·4 |
| p-*Chlorobenzylideneaniline* (*M*, 215·5). | | | | | | | |
| 0·0042378 | 2·2808 | 0·87472 | 1·96 | 0·222 | 1·49779 | 0·33497 | 69·1 |
| 0·0062911 | 2·2845 | 0·87517 | 1·91 | 0·210 | 1·49802 | 0·33497 | 70·1 |
| 0·0079835 | 2·2844 | 0·87548 | 1·99 | 0·217 | 1·49828 | 0·33493 | 69·7 |
| 0·0087396 | 2·2895 | 0·87563 | 1·99 | 0·213 | 1·49833 | 0·33497 | 70·6 |
| p-*Chlorobenzylidene*-p-*toluidine* (*M*, 229·5). | | | | | | | |
| 0·0031769 | 2·2803 | 0·87449 | 2·45 | 0·223 | 1·49770 | 0·33501 | 75·4 |
| 0·0042419 | 2·2805 | 0·87477 | 2·39 | 0·234 | 1·49780 | 0·33497 | 73·6 |
| 0·0045232 | 2·2843 | 0·87484 | 2·61 | 0·234 | 1·49783 | 0·33495 | 72·8 |
| 0·0048470 | 2·2845 | 0·87499 | 2·47 | 0·249 | 1·49786 | 0·33491 | 71·7 |
| 0·0079771 | 2·2901 | 0·87676 | 2·21 | 0·248 | 1·49845 | 0·33458 | 73·9 |
| 0·0107257 | 2·2975 | 0·87694 | 2·33 | 0·207 | 1·49853 | 0·33455 | — |
| p-*Chlorobenzylidene*-p-*chloroaniline* (*M*, 250). | | | | | | | |
| 0·0046280 | 2·2788 | 0·87513 | 1·36 | 0·292 | — | — | — |
| 0·0052943 | 2·2789 | 0·87532 | 1·38 | 0·290 | 1·49781 | 0·33476 | 71·0 |
| 0·0057531 | — | 0·87545 | — | — | 1·49791 | 0·33477 | 72·5 |
| 0·0098592 | 2·2846 | 0·87666 | 1·36 | 0·292 | 1·49823 | 0·33449 | 70·1 |
| 0·0101210 | 2·2863 | 0·87599 | 1·36 | 0·291 | — | — | — |
| 0·0111398 | — | 0·87700 | — | — | 1·49861 | 0·33447 | 71·2 |
| 0·0155380 | 2·2942 | 0·87818 | 1·40 | 0·291 | 1·49871 | 0·33418 | 70·4 |
| *Salicylidene*-m-*toluidine* (*M*, 211). | | | | | | | |
| 0·0058417 | 2·2943 | 0·87490 | 3·71 | 0·192 | 1·49797 | 0·33501 | 69·98 |
| 0·0071484 | 2·3004 | 0·87515 | 3·90 | 0·192 | 1·49821 | 0·33505 | 71·30 |
| 0·0093173 | 2·3078 | 0·87556 | 3·79 | 0·191 | 1·49837 | 0·33499 | 69·79 |
| 0·0100746 | 2·3121 | 0·87572 | 3·93 | 0·192 | 1·49865 | 0·33508 | 71·73 |
| 0·0145614 | 2·3291 | 0·87682 | 3·89 | (0·209) | 1·49914 | 0·33495 | 69·53 |
| 0·0152670 | 2·3305 | 0·87713 | 3·80 | (0·194) | 1·49929 | 0·33491 | 69·03 |
| o-*Methoxybenzylideneaniline* (*M*, 212). | | | | | | | |
| 0·005893 | 2·2988 | 0·87489 | 4·53 | — | 1·49805 | 0·33506 | 72·1 |
| 0·0070782 | — | 0·87518 | — | 0·192 | — | — | — |
| 0·0095929 | 2·3297 | 0·87562 | 5·21 | — | 1·49855 | 0·33507 | 71·0 |
| 0·0103988 | 2·3298 | 0·87575 | 5·50 | — | 1·49859 | 0·33503 | 72·0 |
| 0·0105390 | — | 0·87578 | — | 0·187 | — | — | — |
| 0·0107650 | — | 0·87589 | — | 0·196 | — | — | — |
| 0·0120743 | — | 0·87610 | — | 0·192 | — | — | — |
| 5-*Bromosalicylideneaniline* (*M*, 263). | | | | | | | |
| 0·0018171 | 2·2739 | 0·87433 | (0·77) | (0·303) | 1·49753 | 0·33499 | (93·92) |
| 0·0034715 | 2·2776 | 0·87498 | 1·55 | 0·304 | 1·49773 | 0·33485 | 101·7 |
| 0·0046364 | 2·2797 | 0·87536 | 1·50 | 0·345 | 1·49787 | 0·33477 | 102·9 |
| 0·0071798 | 2·2833 | 0·87626 | 1·50 | 0·345 | 1·49823 | 0·33464 | 100·0 |

frequency and temperature; $\alpha\varepsilon_2$ and $\beta d_2$, the rates of change of dielectric constants and density with weight-fraction, expressed by $\varepsilon_{12} = \varepsilon_2(1 + \alpha w_1)$ and $d_{12} = d_2(1 + \beta w_1)$; $n_D^{25°}$, the refractive index of the solutions for the Na line; $r_{12}$, their specific refractions; and $[R_L]_D$, the corresponding values for the molecular refractions of the solute.

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## 139. *Methylglucosaminide: Its Structure, and the Kinetics of its Hydrolysis by Acids.*

By R. C. G. Moggridge and A. Neuberger.

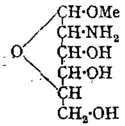
*Consideration of the existing views regarding the structure of methylglucosaminide leads to the conclusion that they are inadequately founded. The betaine structure proposed for this compound by Irvine, McNicoll, and Hynd (J., 1911, **99**, 250; 1912, **101**, 1128) was based on (a) evolution of methylamine on distillation with alkali and (b) abnormal resistance to acid hydrolysis.*

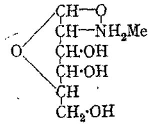
*In this paper a satisfactory alternative explanation of (a) is given; it is further suggested that (b) is compatible with a normal glycosidic structure and is to be explained by the effect of the adjacent positively charged amino-group in repelling hydrions from its immediate vicinity.*

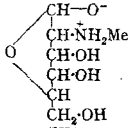
*In order to test this hypothesis N-acetyl methylglucosaminide has been prepared, and a detailed kinetic study has been made of the comparative rates of acid hydrolysis of this compound and of methylglucosaminide.*

*The results are in full accord with the explanation suggested, and it is therefore concluded that methylglucosaminide has in fact a normal glycosidic structure.*

Methylglucosaminide hydrochloride was first prepared by Irvine, McNicoll, and Hynd (*loc. cit.*), who considered that its properties could not be fully explained in terms of the normal glycosidic structure (I), and suggested the presence of a betaine-ring (II). This suggestion was extended both to the structure of the free base, and to mucoproteins (Irvine and Hynd, J., 1913, **103**, 41). [The structure (II) would presumably now be written as a


(I.)


(II.)


(III.)

"zwitterion" (III).] This conclusion seems improbable, and it was thought that a further investigation would be of interest. The chief evidence advanced against the structure (I) was (*a*) the evolution of methylamine on treatment of the compound with alkali, and (*b*) the abnormal difficulty of hydrolysis of the compound by acids, so both these points were reinvestigated.

(*a*) On treatment of the compound with alkali the gases evolved did in fact contain small amounts of methylamine in addition to ammonia, but the conditions necessary for decomposition were extremely drastic, alkaline fusion for 4½ hours at 250° only liberating about half the theoretical amount of alkaline vapours. Less than 10% of the total gaseous nitrogen was in the form of methylamine. Since formaldehyde is produced by the action of alkali on sugars, and methylamine can be formed by the action of formaldehyde on ammonia at high temperature, it seems probable that under the conditions of the experiment methylamine might be formed from a glycoside of structure (I).

(*b*) Methylglucosaminide hydrochloride, as noted by Irvine and Hynd (*loc. cit.*), is hydrolysed much more slowly by acid than is any other known glycoside; but such behaviour can readily be explained by the presence of the charged amino-group in the α-position to the glycoside linkage. Coulomb forces will repel all positively charged ions, and thus decrease considerably the concentration of hydrions in the immediate vicinity of the amino-group, and this will decrease the rate of hydrolysis of the glycoside group, as that reaction is catalysed by hydrions. Analogous cases where reaction velocity is markedly influenced by the introduction of charge are (1) the reaction between thiosulphate and sodium or methyl bromoacetate (LaMer and Kammer, *J. Amer. Chem. Soc.*, 1931, **53**, 2832); (2) the reaction between silver ions and sodium or ethyl bromoacetate (Euler, *Ber.*, 1906, **39**, 2729); (3) the hydrolysis of esters of dicarboxylic acids (Ingold, J., 1935, 1482).

As a first approximation it may be assumed that the velocity constant of the acid-catalysed reaction is proportional to the concentration of hydrogen ions. If $k_0$ is the constant in the absence of any charge effect, $k_1$ that of the charged methylglucosaminide ion, and $C_0$ and $C_1$ the concentration of hydrogen ions respectively in the bulk of the solution and in the immediate surroundings of the glycoside linkage, then

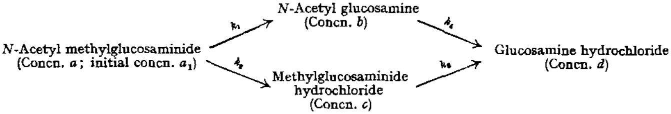
$$k_1 = C_1 k_0 / C_0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Applying the Boltzmann principle, we have, for univalent ions, with $k_0$ and $k_1$ extrapolated to zero ionic strength,

$$k_1 = k_0 e^{-\varepsilon^2/DrkT} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $r$ is the distance of the glycoside linkage from the unit charge $\varepsilon$. It has already been pointed out (Ingold, J., 1931, 2179; Neuberger, *Proc. Roy. Soc.*, 1937, *A*, **158**, 68) that, owing to the difficulty of obtaining a correct value of the dielectric constant in the immediate surroundings of charged groups, the assumptions involved in the derivation of equation (2) are not correct if $r$ is small, and, by analogy with the results obtained with the dissociation constants of dicarboxylic acids and amino-acids, it is to be expected that the value for $r$ calculated from $k_0$ and $k_1$ will be too small.

If this interpretation of the abnormal behaviour of methylglucosaminide hydrochloride on acid hydrolysis is correct, it would be expected that an *N*-acyl methylglucosaminide, which does not carry a charge, should be hydrolysed at a rate comparable with that of ordinary glycosides. *N-Acetyl methylglucosaminide* was prepared to test this conclusion. Its hydrolysis is complicated by the fact that both acetyl and glycoside groups are hydrolysed by acid. We have the following scheme of reactions, all of which should be unimolecular:




In practice it is found that $k_3$ is negligibly small compared with the other constants. The reaction was followed by measuring (1) the free amino-nitrogen ($V$), representing $(c + d)$, by the Van Slyke method, and (2) the reducing power ($R$), representing $(b + d)$, and so the extent of the reaction $k_1$. Under the conditions used, the reducing powers of equimolecular quantities of glucosamine hydrochloride and *N*-acetyl glucosamine were equivalent to within 0·2%. For the reducing powers we have $dR/dt = k_1 a$ and $da/dt = -(k_1 + k_2)a_1$, giving

$$a = a_1 e^{-(k_1 + k_2)t} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

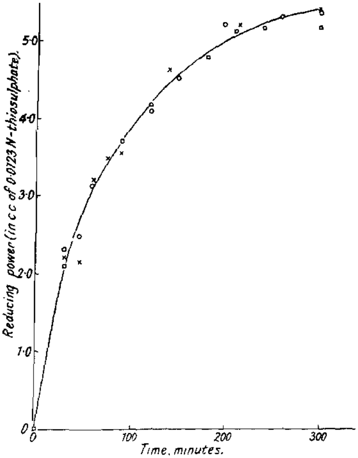
On substituting and integrating, we have

$$R = a_1 k_1 [1 - e^{-(k_1 + k_2)t}]/(k_1 + k_2) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

This was used in the form

$$\frac{(k_1 + k_2)t}{2 \cdot 303} = \log_{10} \frac{a_1 k_1}{k_1 + k_2} - \log_{10}\left(\frac{a_1 k_1}{k_1 + k_2} - R\right) \quad . \quad . \quad . \quad . \quad (5)$$

n approximate value of $a_1k_1/(k_1 + k_2)$ was obtained from the fact that it represents the pparent end-point of the reaction; $t$ was then plotted against the second logarithm in (5) or various values of $a_1k_1/(k_1 + k_2)$, that value giving the best straight line being adopted. he method was found to be sensitive to variations in $a_1k_1/(k_1 + k_2)$ of less than 1%.




*Hydrolysis of N-acetyl methylglucosaminide with* N-HCl *at* 80°. *Theoretical end-point for complete hydrolysis,* 7·45 *c.c.*

For the Van Slyke estimation we have $V = c + d$, $dV/dt = k_2a + k_4b$; further, by equation (3) we have $db/dt = k_1a - k_4b = k_1a_1e^{-(k_1+k_2)t} - k_4b$, giving

$$b = -a_1k_1[e^{-(k_1+k_2)t} - e^{-k_4t}]/(k_1 + k_2 - k_4)$$

Hence $$dV/dt = k_2a_1e^{-(k_1+k_2)t} - \frac{a_1k_1k_4}{k_1 + k_2 - k_4}[e^{-(k_1+k_2)t} - e^{-k_4t}]$$

and on integration

$$V = a_1\{1 - [k_1e^{-k_4t} + (k_2 - k_4)e^{-(k_1+k_2)t}]/(k_1 + k_2 - k_4)\} \quad . \quad . \quad . \quad (6)$$

This expression was used to check the values of $k_1$, $k_2$, and $k_4$ found by other methods.

*N*-Acetyl methylglucosaminide was prepared from tetra-acetyl methylglucosaminide; this could not be obtained crystalline from *tetra-acetobromoglucosamine* (from penta-acetyl glucosamine) but was so obtained by direct acetylation of methylglucosaminide hydrochloride, and later from triacetyl methylglucosaminide hydrobromide, as described by Cutler, Haworth, and Peat (J., 1937, 1979), and on treatment with methyl-alcoholic hydrogen chloride it gave the desired *N*-acetyl methylglucosaminide. An alternative and extremely convenient method of preparation is from penta-acetyl glucosamine. The production of the same compound by these two methods is very hard to explain if the methyl group is associated with the nitrogen, as suggested by Irvine and Hynd (*loc. cit.*). If *O*-tetra-acetyl glucosamine hydrochloride (Bergmann and Zervas, *Ber.*, 1931, **64**, 975) is similarly treated with methyl-alcoholic hydrogen chloride, the product is not methylglucosaminide hydrochloride, but glucosamine hydrochloride.

## EXPERIMENTAL.

*Treatment of Methylglucosaminide with Alkali.*—Methylglucosaminide hydrochloride, prepared by the method of Irvine, McNicoll, and Hynd (*loc. cit.*), was dissolved in 10N-sodium hydroxide and steam-distilled, but gave a negligible amount of alkaline vapours; 0·39 g. was therefore treated with alkali at 250° in a slow current of nitrogen, the gases being passed into hydrochloric acid. About half the calculated amount of alkaline vapours had come over in 4½ hours. The aqueous solution was concentrated to dryness in a vacuum, and the salts purified by one further distillation of the alkaline gases into acid. An almost colourless solid was obtained (Found : C, 3·1; H, 7·7; N, 25·4. Calc. for 82·5% of $NH_4Cl$ + 17·5% of $NH_3MeCl$ : C, 3·1; H, 7·7%; N, 25·2%).

*Tetra-acetobromoglucosamine.*—Penta-acetyl glucosamine—either the crystalline compound (Bergmann and Zervas, *loc. cit.*) or the dry syrup obtained by direct acetylation of glucosamine hydrobromide (10 g.) by means of acetic anhydride and sodium acetate—was dissolved with shaking at room temperature in a solution of hydrogen bromide (15 g.) in glacial acetic acid (30 g.), and left overnight. Chloroform was added, the solution extracted with bicarbonate solution, dried, concentrated to low bnlk, and allowed to evaporate spontaneously. *Tetra-acetobromoglucosamine* (4·9 g.) was deposited as colourless needles, and was recrystallised from glacial acetic acid, $[\alpha]_D$ + 118·2°; it was stable on keeping, but on heating it charred without melting (Found : N, ?·35; Br, 19·7. $C_{14}H_{20}O_8NBr$ requires N, 3·4; Br, 19·5%). Attempts to replace bromine by methoxyl in methyl-alcoholic solution, with pyridine, silver oxide, and silver carbonate as condensing agents, led to uncrystallisable, bromine-free syrups.

*Tetra-acetyl Methylglucosaminide.*—To methylglucosaminide hydrochloride (0·25 g.), suspended in pyridine (7 c.c.), acetic anhydride (7 c.c.) was added slowly at 0°. The clear solution was left in the ice-box overnight, poured into ice-water, and the product crystallised by extraction with chloroform and concentration. From alcohol it formed colourless needles, m. p. 160° (Found : N, 3·8. Calc. : N, 3·9%). A mixed m. p. showed identity with tetra-acetyl methylglucosaminide prepared as described by Cutler, Haworth, and Peat (*loc. cit.*).

N-*Acetyl Methylglucosaminide.*—(a) *From tetra-acetyl methylglucosaminide.* The tetra-acetyl compound (1·25 g.) was refluxed for 2 hours with dry methyl alcohol (30 c.c.) containing hydrogen chloride (2·2% by weight), and the solution then shaken with an excess of lead carbonate, filtered, and concentrated. N-*Acetyl methylglucosaminide* crystallised on standing (yield of once recrystallised material 45%). After three recrystallisations from alcohol it was obtained as colourless needles, m. p. 189°, $[\alpha]_D = + 105°$ (Found: N, 6·05. $C_9H_{17}O_6N$ requires N, 5·95%).

(b) *From penta-acetyl glucosamine.* Glucosamine hydrochloride (2·5 g.) was acetylated in the usual manner by treatment with acetic anhydride and sodium acetate; the dry syrupy product was refluxed with methyl-alcoholic hydrogen chloride (2·2% solution), and the product worked up as above. *N*-Acetyl methylglucosaminide (76% overall yield) crystallised at once; on recrystallisation it was obtained with m. p. 189°, and shown by mixed m. p. to be identical with the substance obtained as in (a).

*Action of Methyl-alcoholic Hydrogen Chloride on* O-*Tetra-acetyl Glucosamine Hydrochloride.*—This compound (3·0 g.) was refluxed with methyl-alcoholic hydrogen chloride (2·2% solution). After about ½ hour, glucosamine hydrochloride (1·5 g.) was deposited as colourless plates (Found : N, 6·55. Calc. : N, 6·5%).

*Kinetic Measurements.*—2-C.c. portions of a solution of the substance under investigation in hydrochloric acid of known strength were sealed into small test-tubes, and suspended in the vapour of a boiling liquid. The tubes were taken out at measured intervals of time, cooled in ice and their contents then estimated either in the Van Slyke apparatus, or by Hanes's modification of the Hagedorn–Jensen method (*Biochem. J.*, 1929, **23**, 99); in the latter case the acid was neutralised before the estimation. The amounts of thiosulphate needed were found to be strictly proportional to the amounts of substance present, being, in c.c. of N/100-solution per mg. of substance :

| | No acid added. | N-HCl experiment. | 2·5N-HCl experiment. |
|---|---|---|---|
| For glucosamine hydrochloride ......... | 2·60 | 2·70 | 3·14 |
| For *N*-acetyl glucosamine ............... | 2·48 | 2·62 | — |

Constants were calculated by Guggenheim's method (*Phil. Mag.*, 1926, **2**, 540), applied to a smooth curve drawn through the experimental points. It is believed that most of the constants for methylglucosaminide hydrochloride are accurate to well within 10%. Blank experiments

showed that there was no appreciable destruction of glucosamine hydrochloride on heating with 2·5N-acid for 65 hours at 100°.

TABLE I.

| Expt. No. | I. | | II. | | III. | | IV. | | V. | | VI. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *t.* | *R.* | *t.* | *R.* | *t.* | *R.* | *t.* | *R.* | *t.* | *R.* | *t.* | *R.* |
| | 1 | 0·24 | 1 | 0·43 | 24 | 0·82 | 2 | 0·17 | 0·5 | 0·78 | 2 | 0·70 |
| | 3 | 1·30 | 2 | 0·91 | 48 | 1·51 | 4 | 0·24 | 1·0 | 1·60 | 4 | 1·22 |
| | 5 | 1·93 | 3 | 1·17 | 72 | 2·43 | 6 | 0·28 | 1·5 | 2·37 | 6 | 2·00 |
| | 7 | 2·45 | 4 | 1·60 | 81 | 2·89 | 10 | 0·75 | 2·0 | 2·68 | 8·5 | 2·48 |
| | 8 | 2·70 | 5 | 1·93 | 95 | 3·02 | 24 | 1·26 | 2·5 | 3·50 | 10 | 2·68 |
| | 8·5 | 2·95 | 6 | 2·29 | 149 | 4·33 | 35 | 1·94 | 3 | 3·94 | 12 | 2·76 |
| | 9 | 2·94 | 8 | 2·71 | | | 52 | 2·26 | 4 | 4·40 | 22 | 3·95 |
| | 10 | 3·10 | 11 | 3·64 | | | 72 | 2·47 | 5 | 4·90 | 25 | 4·15 |
| | 11 | 3·40 | | | | | | | 6 | 5·33 | 29 | 4·59 |
| Theoretical end-points | | 7·30 | | 7·30 | | 7·30 | | 6·25 | | 7·30 | | 8·55 |

*Hydrolysis of methylglucosaminide hydrochloride.* The data are in Table I : $t$ = time in hours; $R$ = equivalent of reducing sugar in c.c. of 0·01233N-thiosulphate; 3·02 mg. of substance used in each reading in experiments I—V, and 4·12 mg. in experiment VI.

Expts. I & II (duplicate) : 2·5N-acid at 100°. $k = 2·08 \times 10^{-5}$ (sec.$^{-1}$).
Expt. III : 2·5N-Acid at 80° (benzene). $k = 1·585 \times 10^{-6}$.
,, IV : N-Acid at 100°. $k = 4·05 \times 10^{-6}$.
,, V : 2·5N-Acid at 110·8° (fractionated toluene). $k = 7·95 \times 10^{-5}$.
,, VI : N-Acid at 110·8°. $k = 1·83 \times 10^{-5}$.

TABLE II.

| Expt. No. | VII. | | VIII. | | IX. | | X. | | XI. | | XII. | | XIII. | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *t.* | *R.* | *t.* | *R.* | *t.* | *R.* | *t.* | *R.* | *t.* | *R.* | *t.* | *V.* | *t.* | *V.* | *V'.* |
| | 30 | 2·12 | 30 | 2·23 | 30 | 2·33 | 15 | 3·62 | 2 | 1·16 | 1 | 0·72 | 1 | 0·46 | 0·28 |
| | 90 | 3·71 | 45 | 2·17 | 45 | 2·50 | 19 | 3·78 | 4 | 1·94 | 2 | 1·16 | 2 | 0·82 | 0·59 |
| | 120 | 4·20 | 60 | 3·22 | 60 | 3·13 | 23 | 3·90 | 8 | 3·00 | 2·5 | 1·22 | 2·5 | 0·93 | 0·75 |
| | 180 | 4·83 | 75 | 3·50 | 120 | 4·13 | 39 | 4·35 | 25 | 4·20 | 3·0 | 1·31 | 3·0 | 1·01 | 0·87 |
| | 210 | 5·18 | 90 | 3·58 | 150 | 4·57 | 42 | 4·36 | 30 | 4·34 | 3·5 | 1·46 | 3·5 | 1·12 | 0·99 |
| | 240 | 5·22 | 140 | 4·79 | 200 | 5·27 | 45 | 4·50 | 48 | 4·48 | 4·5 | 1·59 | 4·5 | 1·28 | 1·16 |
| | 300 | 5·24 | 215 | 5·25 | 260 | 5·37 | 63 | 4·45 | 54 | 4·60 | | | 5·5 | 1·35 | 1·32 |
| | | | 300 | 5·47 | 300 | 5·43 | 65 | 4·45 | | | | | | | |
| | | | | | | | 67 | 4·53 | | | | | | | |
| Theoretical end-points | | 7·45 | | 7·45 | | 7·45 | | 7·45 | | 7·45 | | 1·94 | | 1·61 | 1·61 |

*Hydrolysis of* N-*acetyl methylglucosaminide.* 3·65 Mg. of substance per reading ($R$ as before).

Expts. VII, VIII, and IX (triplicate; see fig.) : N-acid at 80° (benzene) ; $t$ in minutes.
$k_1$ (glycoside hydrolysis) = $1·21 \times 10^{-4}$; $k_2$ (acetyl hydrolysis) = $3·55 \times 10^{-5}$.
Expts. X and XI (duplicate) : N-acid at 61·25° (chloroform) ; $t$ in hours.

$$k_1 = 1·25 \times 10^{-5};\ k_2 = 8 \times 10^{-6}.$$

*Van Slyke estimations.* (i) On $N$-acetyl glucosamine (Expt. XII).—30·6 Mg. per reading; $t$ in hours; $V$ in mg. of amino-nitrogen; N-acid at 80°. $k_4 = 1·3 \times 10^{-4}$.

(ii) On $N$-acetyl methylglucosaminide (Expt. XIII).—27 Mg. per reading; $t$ in hours; $V$ in mg. of amino-nitrogen; N-acid at 80°. $V'$ = readings as calculated from equation (6) with $k_1 = 1·2 \times 10^{-4}$, $k_2 = 3·7 \times 10^{-5}$, $k_4 = 1·3 \times 10^{-4}$. The agreement between $V$ and $V'$ is as good as could be expected.

## DISCUSSION OF RESULTS.

Tables I and II show that methylglucosaminide hydrochloride is hydrolysed very much more slowly by acids than is N-acetyl methylglucosaminide, the glycoside linkage of the latter being, as is expected, split at a rate comparable with that of ordinary pyranosides. The figure shows the characteristic curve to be expected for the hydrolysis of N-acetyl methylglucosaminide, the rate of formation of reducing sugar being initially rapid, but

becoming slower as the acetyl group is hydrolysed off to give the relatively very stable methylglucosaminide hydrochloride.

Values for the energies of activation can be calculated from the constants at different temperatures. For methylglucosaminide hydrochloride we have three independent readings; from Expts. I, II, and V, $E = 35{,}200$ cals.; from I, II and III, $E = 36{,}300$ cals.; from IV and VI, $E = 39{,}600$ cals. The accuracy in the particular case of Expt. IV is probably not more than 15% and this error is more than enough to account for the deviation in the last value of $E$. Probably the best value is about 36,000 cals.

For *N*-acetyl methylglucosaminide we have $E$ (glycoside hydrolysis) = 28,400 cals., $E$ (acetyl hydrolysis) = 19,200 cals. Most simple pyranosides have energies of activation of 28,000—34,000 cals.; these values then provide some confirmation, though of course no proof, for the assumption generally made that these glucosamine derivatives have a pyranoside ring structure. The energy of activation for the hydrolysis of methylglucosaminide is only a few thousand calories higher than for its uncharged analogues; so the main effect of the charge on the equation $k = PZ\varepsilon^{-E/RT}$ is to increase the $PZ$ term.

All the constants refer to systems of high ionic strength; the collision between hydrions and the positively charged methylglucosaminide ions leads to a doubly charged complex, and the salt effect is therefore expected to be much larger for this reaction than for the hydrolysis of glycosides in general. The existence of a large salt effect is shown by the fact that at a given temperature the values of the hydrolysis constants are not proportional to the hydrion concentrations; a 2·5-fold increase of acid strength causes a nearly 5-fold increase of constant. For strict quantitative comparison the constants should be extrapolated to zero ionic strength; this, however, proved impossible owing to the stability of the glycoside linkage in methylglucosaminide hydrochloride, the hydrolysis being impracticably slow at acid concentrations of less than N, even at 110°. A further difficulty is that the configuration of methylglucosaminide hydrochloride is unknown, though from the work of Cutler, Haworth, and Peat (*loc. cit.*) it seems probable that the *N*-acetyl methylglucosaminide has been converted into the α-form by the use of methyl-alcoholic hydrogen chloride.

These two factors make a quantitative comparison of the hydrolysis constants of the charged and uncharged glycosides difficult; neither, however, would be expected to be large enough appreciably to affect the order of magnitnde of the ratio of constants. If it is assumed that the variation of the constant with acid concentration is independent of the temperature, a constant of approximately $3{\cdot}5 \times 10^{-7}$ is found for methylglucosaminide in N-acid at 80°. Under these conditions the constants for *N*-acetyl methylglucosaminide, α- and β-methylglucosides (Moelwyn-Hughes, *Trans. Faraday Soc.*, 1929, **25**, 503) are approximately 350, 100, and 180 times higher respectively. Now at 80°, using the values of Wyman (*Physical Rev.*, 1930, **35**, 623) for the dielectric constant of water, equation (2) becomes $k_0/k_1 = 3{\cdot}39/r$, $r$ being the distance (in A.) between the charge and the glycoside linkage. Substituting for $k_0/k_1$ the constant-ratios given above, the valnes of 1·3, 1·7, and 1·5 A. are obtained. These distances are certainly of the right order of magnitude.

It appears therefore that the conception of inhibition of acid catalysis by the charged amino-group provides an adequate explanation of the abnormal stability of methylglucosaminide towards acids. It can also explain (1) the fact that glucosamine alone, of all monosaccharides, is not converted into a glycoside by treatment with methyl-alcoholic hydrogen chloride; (2) the contrast between the behaviours of penta-acetyl glucosamine and *O*-tetra-acetyl glucosamine hydrochloride on treatment with methyl-alcoholic hydrogen chloride—the former gives *N*-acetyl methylglucosaminide, whereas the latter gives glucosamine hydrochloride, no glycoside formation having taken place.

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# 140. *A Preparation of* m-*Dimethylaminobenzaldehyde. Part II.*

By WESLEY COCKER, J. O. HARRIS, and (in part) J. V. LOACH.

The method used by Bottomley, Cocker, and Nanney (J., 1937, 1891) for the preparation of *m*-dimethylaminobenzaldehyde has been superseded by a method in which *m*-nitrobenzaldehyde dimethylacetal is reduced in aqueous solution with sodium sulphide to *m*-aminobenzaldehyde dimethylacetal and then methylated with methyl sulphate. The quaternary salt is decomposed by hot caustic potash solution, and *m*-dimethylaminobenzaldehyde obtained in yields exceeding 70%, calculated on the *m*-nitrobenzaldehyde used.

THE preparation of the acetal of *m*-aminobenzaldehyde previously described (*loc. cit.*) required the use of somewhat costly materials. It has now been found simpler to reduce *m*-nitrobenzaldehyde dimethylacetal with aqueous sodium sulphide (compare Haworth and Lapworth, J., 1922, **121**, 76), since this acetal can be obtained in almost theoretical yield by the method of Voss and Blanke (*Annalen*, 1931, **485**, 271). No trace of *m*-dimethylaminobenzaldehyde dimethylacetal was found at any stage of the reaction, nor have we been able to prepare it by any of the known methods from *m*-dimethylaminobenzaldehyde, and it appears that even in alkaline solution it is incapable of existence.

Unlike the acetal of *m*-aminobenzaldehyde, *m*-nitrobenzaldehyde dimethylacetal is stable for short periods even in presence of mineral acid. This is not in disharmony with the known order of electron-releasing effects of $NMe_2$, $NH_2$, and $NO_2$ and the accepted mechanism of the decomposition of acetals, even though the acetal group be in the *m*-position to these groups.

*m*-Dimethylaminobenzaldehyde is unaffected even by prolonged boiling with concentrated caustic potash solution (compare Clemo and Smith, J., 1928, 2423, on *p*-dimethylaminobenzaldehyde). Attempts to prepare a " benzoin " from it have been futile, nor was it possible to prepare a " mixed benzoin " with piperonal, although Buck and Ide (*J. Amer. Chem. Soc.*, 1931, **53**, 2353) record the preparation of similar compounds from *p*-dimethylaminobenzaldehyde. In all our experiments along these lines the aldehyde was recovered quantitatively unchanged. In addition we have been unable to form a bisulphite compound. This evidence points to the feeble additive power of the carbonyl groups for anionoidal reagents.

*o*-Dimethylaminobenzaldehyde was similarly obtained from *o*-nitrobenzaldehyde, but the yields were only about 40% of the theoretical. Deacetalisation took place during methylation, but in addition, although a considerable excess of methyl sulphate over the theoretical quantity required for quaternary salt formation was used, the methylation apparently stopped at the tertiary amine stage. Possibly the presence of the *o*-aldehydo-group is responsible for this.

## EXPERIMENTAL.

m-*Nitrobenzaldehyde Dimethylacetal.*—A mixture of *m*-nitrobenzaldehyde (76 g.), methyl sulphite (60 g.), and methyl alcohol (60 c.c.) was treated with a trace of dry hydrogen chloride and refluxed on the water-bath for 8 hours, sulphur dioxide being evolved as acetalisation took place. The homogeneous mixture was poured into a solution of sodium methoxide (sodium, 2 g.; methyl alcohol, 40 c.c.) to neutralise free acid present, and the excess of methyl sulphite decomposed by shaking for ½ hour with 15% sodium hydroxide solution (200 c.c.). The mixture was diluted to 1000 c.c. with water, and the acetal extracted with ether and washed with water. After removal of solvent the acetal was normally reduced without purification, but it may be purified by drying over sodium sulphate and distillation in a vacuum; b. p. 159°/20 mm. Yield, 96—98 g. or 97% of the theoretical (compare Claisen, *Ber.*, 1898, **31**, 1016; Haworth and Lapworth, *loc. cit.*).

m-*Aminobenzaldehyde Dimethylacetal.*—The above acetal was reduced by a modification of a method of Haworth and Lapworth. It was slowly poured down a condenser into a hot agitated mixture prepared from crystalline sodium sulphide (300 g. in 300 c.c. of water) and concentrated hydrochloric acid (125 g.). Reaction commenced almost immediately and was completed by boiling for a further 8 hours. The crude acetal was extracted with ether and washed with water.

*Methylation.* The ethereal extracts from the above, containing about 70 g. of crude acetal, were shaken with 300 c.c. of 7% sodium carbonate solution and 20 g. of methyl sulphate for 8 hours, and the process continued by the addition at 8-hour intervals of further similar quantities of methyl sulphate and sodium carbonate until 220 g. of methyl sulphate (1·7 mols.) had been added. The ethereal layer was separated, and the alkaline layer concentrated to about 500 c.c. It was then treated with 500 g. of solid caustic potash, with cooling to prevent loss of *m*-dimethylaminobenzaldehyde, which separated as an upper oily layer as the potash dissolved. The mixture was distilled, water being added to keep the volume constant. The aldehyde was extracted from the distillate with ether, dried (anhydrous potassium carbonate), and distilled in a vacuum. The yield was 46 g. (74% of the theoretical, calc. on the *m*-nitrobenzaldehyde); b. p. 112°/7 mm. The aldehyde thus prepared corresponded in all its properties with that prepared by the method described in Part I (*loc. cit.*). It gave a semicarbazone, m. p. 228—229° (Found: N, 27·0. Calc. for $C_{10}H_{14}ON_4$: N, 27·2%), and an oxime, m. p. 75—76° (Found: C, 65·9; H, 7·2; N, 17·1. Calc. for $C_9H_{12}ON_2$: C, 65·85; H, 7·3; N, 17·1%). The 2 : 4-*dinitrophenylhydrazone hydrochloride* formed scarlet, ill-defined crystals, m. p. 231° (decomp.), from 25% hydrochloric acid (Found: N, 18·6; Cl, 9·4. $C_{15}H_{15}O_4N_5$,HCl requires N, 19·15; Cl, 9·7%). When heated with water, this rapidly lost hydrogen chloride and became oily, possibly yielding the free 2 : 4-dinitrophenylhydrazone and some free aldehyde. The *chloroplatinate* was deposited from hot water in transparent red-yellow needles, m. p. 167—168° (decomp. on rapid heating) (Found: C, 29·2; H, 3·75; Pt, 26·3. $2C_9H_{11}ON,H_2PtCl_6,2H_2O$ requires C, 29·1; H,3·2; Pt, 26·3%).

3 : 3′-*Bisdimethylaminobenzylideneazine*.—A mixture of *m*-dimethylaminobenzaldehyde (1 g.), hydrazine sulphate (2 g.), and alcohol (5 c.c.) was refluxed for 15 minutes, cooled, and treated with 15% caustic soda solution to remove sulphuric acid. The yellow precipitate, recrystallised from alcohol, formed large, transparent, flat, square plates, m. p. 153—154° (Found: N, 19·1. $C_{18}H_{22}N_4$ requires N, 19·2%).

m-*Dimethylaminobenzylideneacetophenone*, obtained from the aldehyde (1 g.), acetophenone (0·8 g.), alcohol (10 c.c.) and 15% caustic soda solution (1 c.c.) after 24 hours at room temperature, gave tufts of bright orange, rectangular plates, m. p. 108—109°, from 95% alcohol, readily soluble in benzene (Found: C, 81·4; H, 6·6; N, 5·8. $C_{17}H_{17}ON$ requires C, 81·3; H, 6·8; N, 5·6%).

6-*Nitroso*-m-*dimethylaminobenzaldehyde*, obtained by addition of sodium nitrite solution to an ice-cold solution of *m*-dimethylaminobenzaldehyde in N-hydrochloric acid, formed masses of bright yellow needles, m. p. 129·5—130°, from 95% alcohol (Found: N, 15·6. $C_9H_{10}O_2N_2$ requires N, 15·7%). It had a peppery odour and was readily soluble in concentrated hydrochloric acid, from which caustic soda precipitated it. The fact that the nitroso-group is in the *p*-position to the dimethylamino-group was confirmed by conversion into the corresponding "methylene-blue."

*Crystal-violet Analogue*.—*m*-Dimethylaminobenzaldehyde (2 g.), dimethylaniline (3·3 g.), and anhydrous zinc chloride (3·3 g.) were heated with stirring in an open dish for 5½ hours. The excess of volatile reagents was removed in steam, and the residual brown-yellow solid washed with water, dried, and recrystallised from absolute alcohol. The *leuco-base* (3·1 g.; 62% of the theoretical yield) formed long, green-yellow, transparent prisms, m. p. 149—149·5° (Found: C, 80·1; H, 8·2; N, 11·3. $C_{25}H_{31}N_3$ requires C, 80·4; H, 8·3; N, 11·3%). It was readily oxidised by lead peroxide to the colour base, which was intermediate in colour between malachite-green and crystal-violet.

The leuco-base prepared from diethylaniline and *m*-dimethylaminobenzaldehyde was obtained from alcohol as green-yellow, transparent prisms, m. p. 72—73·5°. It was readily oxidised to the deep green-violet colour base.

*Attempted "Benzoin" Formation*.—1. A mixture of *m*-dimethylaminobenzaldehyde (6 g.), potassium cyanide (3 g.), and alcohol (20 c.c.) was refluxed for 3 hours, cooled, and kept for 2 days. No crystals were deposited. Water was then added, and the precipitated oil extracted with ether. Yield, 7 g. Converted into semicarbazone, it gave an 80% yield of almost pure *m*-dimethylaminobenzaldehydesemicarbazone, indicating almost complete recovery of aldehyde.

2. A mixture of the aldehyde (3 g.), piperonal (3 g.), potassium cyanide (2 g.), and alcohol (15 c.c.) was refluxed for 3 hours. After 3 days the deposit was collected (0·9 g., m. p. 118—119°). It gave no depression of m. p. with piperoin. The alcoholic residue was diluted with water, and the oil extracted with ether. The extract, washed with hydrochloric acid, yielded 1·2 g. of piperonal and 2·5 g. of the aldehyde. Similar results were obtained when *m*-dimethylaminobenzaldehyde, benzoin, and potassium cyanide were heated together in alcohol. All the

reactants were recovered unchanged (compare Buck and Ide, *J. Amer. Chem. Soc.*, 1931, **53**, 2785).

*Experiments on the Preparation of* o-*Dimethylaminobenzaldehyde*.—Using *o*-nitrobenzaldehyde (38 g.), methyl sulphite (30 g.), and methyl alcohol (30 c.c.) with a trace of dry hydrogen chloride as catalyst, we obtained the acetal in a yield of 45 g. (92% of the theoretical), b. p. 141—144°/15 mm. (compare Fischer, *Ber.*, 1897, **30**, 3053; 1898, **31**, 345). On reduction as described previously, 30 g. of *o*-aminobenzaldehyde dimethylacetal were obtained as a pale yellow liquid, which readily reverted to the free aldehyde even in the absence of acid (compare Freundler and De Laborderie, *Bull. Soc. chim.*, 1907, **1**, 234).

The methylation was carried out with methyl sulphate (115 g.; 1·7 mols.). After 2 days the ethereal layer was removed and distilled in steam, yielding crude *o*-dimethylaminobenzaldehyde. On distillation in a vacuum it yielded 12 g. (37% of the theoretical) of a pale yellow oil, b. p. 132°/25 mm. This was almost pure aldehyde. The aqueous layer from the methylation was concentrated to about 300 c.c., treated with 300 g. of solid caustic potash, and distilled. No oil passed over, but the aqueous distillate gave about 1 g. of aldehyde on continuous extraction with ether. Similarly the strongly alkaline solution yielded only a trace of oil.

*o*-Dimethylaminobenzaldehyde yielded a bisulphite compound after 2 hours' shaking with saturated sodium bisulphite. This yielded pure aldehyde on distillation with sodium carbonate solution. The *semicarbazone* crystallised from a large amount of alcohol in clusters of colourless transparent prisms, m. p. 224—225° (decomp.) (Found: N, 27·2. $C_{10}H_{14}ON_4$ requires N, 27·2%). The aldehyde yielded 2 : 2'-bisdimethylaminobenzylideneazine, m. p. 148—149° (Cohn, *Monatsh.*, 1904, **25**, 371) (Found: N, 18·9. Calc. for $C_{18}H_{22}N_4$: N, 19·0%).

o-*Dimethylaminobenzylideneacetophenone* separated from 95% alcohol in yellow, six-sided, pointed prisms, m. p. 66—67° (Found: N, 5·9. $C_{17}H_{17}ON$ requires N, 5·6%).

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## 141. *The Synthesis of Phenyl- and Pyridyl-glyoxalines.*

By George Roger Clemo, Thomas Holmes, and Grace Cumming Leitch.

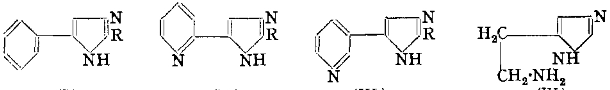
In view of the great physiological interest attached to histidine and histamine, and in continuation of the work done here on pyridylpyrazoles, it was decided to synthesise 5(4)-3'-*pyridylglyoxaline* (III, R = H), which incorporates the structure of histamine, and the isomeric 5(4)-2'-*pyridylglyoxaline* (II, R = H). They were obtained from ethyl nicotinate and picolinate respectively, by preparing the 3- and the 2-ω-aminoacetylpyridine, which were then condensed with potassium thiocyanate to give the glyoxaline thiols. The latter were oxidised by nitric acid to give (III) and (II) respectively.

The physiological importance of the glyoxaline nucleus, as exemplified by the purines, histidine, histamine, the closely related ergothionine, and the pilocarpine alkaloids, has led in the past to considerable work in this field.

In view of the fact that 5(4)-3'-pyridylglyoxaline (III, R = H) incorporates the structure of histidine and histamine (IV), and furthermore also contains the skeleton of the very important nicotinic acid amide, it was decided to continue the work on pyridylpyrazoles (J., 1934, 1739) by preparing it from 3-acetylpyridine.

Syntheses of this type have been much facilitated by the use of the new method of making ω-aminoacetophenone and related compounds (Neber and Huh, *Annalen*, 1935, **515**, 283). The various reactions were tested with acetophenone, which was first converted into ω-aminoacetophenone hydrochloride, and thence into 5(4)-*phenylglyoxaline-2-thiol* (I, R = SH) by treatment with potassium thiocyanate. The thiol group was removed by oxidation with dilute nitric acid, 5(4)-phenylglyoxaline (I, R = H), identical with that described by Pinner (*Ber.*, 1902, **35**, 4135), being obtained.

A similar treatment of 2- and 3-acetylpyridines gave 5(4)-2'-*pyridylglyoxaline* and 5(4)-3'-*pyridylglyoxaline* respectively.



(I.) (II.) (III.) (IV.)

## Experimental.

5(4)-*Phenylglyoxaline-2-thiol*.—ω-Aminoacetophenone hydrochloride (2 g.) (Neber and Huh, *loc. cit.*) was dissolved in water (10 c.c.) and treated with potassium thiocyanate (2 g.). The solution was heated on the water-bath for ½ hour, and treated, after cooling, with an excess of sodium bicarbonate. The precipitated *thiol* crystallised from benzene–alcohol (4 : 1) in colourless plates, m. p. 267·5° (Found: C, 61·1; H, 4·9. $C_9H_8N_2S$ requires C, 61·4; H, 4·5%). The *picrate* separated from alcohol in yellow plates, m. p. 177° (Found: C, 45·6; H, 3·9; N, 15·4. $C_9H_8N_2S,C_6H_3O_7N_3,C_2H_5{\cdot}OH$ requires C, 45·2; H, 3·8; N, 15·5%).

*Phenacylthiourea* (1·25 g.), obtained on concentration of the above bicarbonate solution, crystallised from benzene–alcohol (1 : 1) in colourless needles, m. p. 136° (Found: C, 56·3; H, 5·4. $C_9H_{10}ON_2S$ requires C, 55·7; H, 5·2%). On treatment with an alcoholic solution of picric acid it gave a picrate identical with that obtained from 5(4)-phenylglyoxaline-2-thiol, this treatment being sufficient to complete the condensation. M. p. (alone, and mixed with authentic picrate from the glyoxaline) 177°.

5(4)-*Phenylglyoxaline*.—The thiol (0·4 g.) was added slowly to 22 c.c. of 10% nitric acid on the water-bath, and the whole was heated under reflux for 1 hour. On cooling, the glyoxaline nitrate, m. p. 168°, separated. On treatment of the nitrate with an excess of sodium bicarbonate solution, phenylglyoxaline, m. p. 127°, identical with that already described (*loc. cit.*) was obtained.

*Ethyl Picolinoylacetate*.—Finely divided potassium (5 g.), suspended in benzene (150 c.c.), was treated with dry ethyl alcohol (7·5 c.c.) and, after cooling, with ethyl picolinate (10 g.), followed by ethyl acetate (20 c.c.). The mixture was heated on the water-bath under reflux for 6 hours, and diluted with water; hydrochloric acid (1 : 1) was added, and the ethyl picolinoylacetate liberated by the addition of excess of sodium bicarbonate. The benzene layer, containing the ester, was separated, and the aqueous layer extracted several times with benzene. The benzene extract was dried over sodium sulphate and fractionated under reduced pressure, giving ethyl picolinoylacetate (6 g.), b. p. 150°/2 mm. (decomp.).

5-2'-*Pyridylpyrazolone*.—Ethyl picolinoylacetate (1·5 g.) was refluxed for 5 hours on the water-bath with hydrazine hydrate (2 c.c.) in methyl alcohol (8 c.c.). The solution was evaporated to dryness under reduced pressure, and the residue dissolved in water and a slight excess of acetic acid, giving 5-2'-*pyridylpyrazolone* (0·9 g.), m. p. 219° after recrystallisation from alcohol (Found: C, 59·7; H, 4·7. $C_8H_7ON_3$ requires C, 59·6; H, 4·4%).

2-*Acetylpyridine*.—In subsequent preparations of ethyl picolinoylacetate, on completion of the condensation, the benzene was removed under reduced pressure, and dilute hydrochloric acid (130 c.c.; 1 : 1) added. The resulting solution was refluxed for 4 hours and cooled, excess of solid sodium bicarbonate added, and the liquid extracted with benzene. The extract was dried over sodium sulphate and fractionated under reduced pressure, giving 2-acetylpyridine (4 g.), b. p. 78°/12 mm. The oxime melted at 120°, as described in the literature.

O-p-*Toluenesulphonyl-2-acetylpyridineoxime*.—The oxime (7·4 g.) in pyridine (15 c.c.) was cooled in a freezing mixture and treated with finely powdered *p*-toluenesulphonyl chloride (11·3 g.). The mixture was kept overnight and then poured into a mixture of ice and water. The O-p-*toluenesulphonyl* ester, which separated, was filtered off, dried in a vacuum (15·8 g.), and crystallised from alcohol by dilution with water; m. p. 81—82° (Found: C, 58·2; H, 4·9. $C_{14}H_{14}O_3N_2S$ requires C, 57·9; H, 4·8%).

2-(ω-*Aminoacetyl*)*pyridine Hydrochloride*.—Potassium (2·45 g.) was dissolved in dry alcohol (60 c.c.), and the *p*-toluenesulphonyl ester (15·8 g.), in dry alcohol (40 c.c.), added. The mixture was shaken for 1 hour, and the precipitate of potassium *p*-toluenesulphonate removed. The filtrate was diluted with dry ether (800 c.c.), and a further precipitate of the potassium salt filtered off. The filtrate was extracted three times with 2N-hydrochloric acid (200 c.c.), and the combined extracts evaporated to dryness at 30—40° under reduced pressure, giving 2-(ω-

*aminoacetyl)pyridine hydrochloride* (11 g.), which crystallised from alcohol in colourless, stout prisms, m. p. 171—172° (decomp.) (Found: C, 48·7; H, 5·2. $C_7H_8ON_2$,HCl requires C, 48·7; H, 5·2%).

*5(4)-2′-Pyridylglyoxaline-2-thiol* (II, R = SH).—2-(ω-Aminoacetyl)pyridine hydrochloride (2·5 g.) in water (10 c.c.) was treated with potassium thiocyanate, the solution then being heated for 3 minutes on the water-bath. On cooling, *5(4)-2′-pyridylglyoxaline-2-thiol hydrochloride* separated (1·9 g.); it crystallised from dilute alcohol (4 : 1), containing a trace of hydrochloric acid, in yellow prisms, m. p. 303° (decomp.) (Found: C, 45·3; H, 4·0. $C_8H_7N_3S$,HCl requires C, 45·0; H, 3·8%). The thiol hydrochloride (1·9 g.) on treatment with excess of sodium bicarbonate solution gave the free *thiol* (1·4 g.), which crystallised from alcohol in colourless prisms, m. p. 247—248° (Found: C, 54·5; H, 4·5; N, 23·5. $C_8H_7N_3S$ requires C, 54·2; H, 4·0; N, 23·7%). The *picrate* crystallised from alcohol in long yellow needles, m. p. 194—195° (Found: C, 43·1; H, 4·1; N, 16·9. $C_8H_7N_3S,C_6H_3O_7N_3,2C_2H_5{\cdot}OH$ requires C, 43·4; H, 4·4; N, 16·9%).

*5(4)-2′-Pyridylglyoxaline* (II, R = H).—The thiol (0·2 g.) was added in small portions to hot nitric acid (1·5 c.c.) in water (10 c.c.), and the solution heated on the water-bath for 1 hour. After cooling, excess of sodium bicarbonate was added, the solution evaporated to dryness, and the residue extracted with dry ether. On concentration of the extract and addition of light petroleum until the solution was cloudy, irregular prisms were obtained, m. p. 112° (Found: C, 66·05; H, 4·8; N, 29·3. $C_8H_7N_3$ requires C, 66·2; H, 4·8; N, 29·0%). The compound was easily soluble in cold water, giving a solution alkaline to litmus. The *picrate* of *5(4)-2′-pyridylglyoxaline* was formed in alcohol and crystallised from acetone; m. p. 207—208° (Found: C, 40·1; H, 2·2; N, 20·4. $C_8H_7N_3,2C_6H_3O_7N_3$ requires C, 39·8; H, 2·15; N, 20·9%).

O-p-*Toluenesulphonyl-3-acetylpyridineoxime*.—This *ester* (10·3 g.), obtained from 3-acetylpyridineoxime (5 g.) (J., 1934, 1739), pyridine (15 c.c.), and *p*-toluenesulphonyl chloride (7·5 g.) (see the corresponding 2-acetyl compound), crystallised from alcohol, on dilution with water, in colourless plates, m. p. 78° (Found: C, 57·8; H, 4·8; S, 11·2. $C_{14}H_{14}O_3N_2S$ requires C, 57·9; H, 4·9; S, 11·0%).

*3-(ω-Aminoacetyl)pyridine Hydrochloride*.—Potassium (0·3 g.) was dissolved in dry alcohol (5 c.c.), and the preceding ester (2 g.) added. The mixture was shaken for 1 hour, the precipitate of potassium *p*-toluenesulphonate filtered off, both before and after addition of dry ether (120 c.c.), and the ethereal solution extracted three times with 2N-hydrochloric acid (13 c.c.). The combined extract was evaporated to dryness at 30—40° under reduced pressure, giving *3-(ω-aminoacetyl)pyridine dihydrochloride* (1·1 g.), which crystallised from alcohol–acetone in colourless needles, m. p. 172° (decomp.) (Found: C, 40·7; H, 4·9; Cl, 33·0. $C_7H_8ON_2$,2HCl requires C, 40·2; H, 4·8; Cl, 34·0%).

*5(4)-3′-Pyridylglyoxaline-2-thiol* (III, R = SH).—3-(ω-Aminoacetyl)pyridine hydrochloride (1·1 g.) in water (6 c.c.) was treated with potassium thiocyanate (0·7 g.), and the resulting solution heated on the water-bath for ½ hour. On cooling, *5(4)-3′-pyridylglyoxaline-2-thiol hydrochloride* separated (0·4 g.); it crystallised from dilute alcohol in long lemon-yellow prisms, m. p. 241—242° (Found: C, 45·8; H, 4·2. $C_8H_7N_3S$,HCl requires C, 45·0; H, 3·8%). The free *base*, liberated by treatment with sodium bicarbonate solution (1·1 g. of hydrochloride gave 0·85 g. of free base), crystallised from alcohol in clusters of stout prisms, m. p. 291—292° (Found: C, 54·3; H, 4·4. $C_8H_7N_3S$ requires C, 54·2; H, 4·0%).

*5(4)-3′-Pyridylglyoxaline* (III, R = H).—The thiol (0·5 g.) was added in small portions to hot nitric acid (3·75 c.c.) in water (25 c.c.), and the solution heated on the water-bath for 1 hour. On cooling, 0·61 g. of the *dinitrate* of (III, R = H) separated, m. p. 200° (decomp.) after crystallisation from alcohol (Found: C, 35·6; H, 3·0. $C_8H_7N_3,2HNO_3$ requires C, 35·4; H, 3·3%). On treatment of this with sodium bicarbonate solution, followed by evaporation to dryness and extraction of the residue with ether, *5(4)-3′-pyridylglyoxaline* was obtained as a colourless solid, m. p. 117—118°, after recrystallisation from ether and light petroleum (Found: C, 66·1; H, 4·7; N, 28·5. $C_8H_7N_3$ requires C, 66·2; H, 4·8; N, 29·0%). The compound was easily soluble in cold water, giving a solution alkaline to litmus.

The *picrate* was formed in alcohol and recrystallised from glacial acetic acid, in which it was sparingly soluble, separating in warts, decomp. 285° (Found: C, 44·65; H, 2·55. $C_8H_7N_3,C_6H_3O_7N_3$ requires C, 44·9; H, 2·7%).

Our thanks are due to the Medical Research Council for a grant, and to Mr. W. A. Campbell for micro-analyses.

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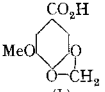
[*Received, April 1st, 1938.*]

# 142. *The Constitution of Croweacin.*

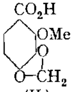
By A. R. PENFOLD, G. R. RAMAGE, and J. L. SIMONSEN.

The phenolic ether, croweacin, $C_{11}H_{12}O_3$, occurring in the essential oil from the leaves and terminal branchlets of *Eriostemon crowei* (*Crowei saligna*) has been shown to be represented by (VII), since it yields on oxidation croweacic acid, $C_9H_8O_6$, shown by synthesis to be 2-*methoxy*-3 : 4-*methylenedioxybenzoic acid* (II), and a glycol oxidisable by lead tetra-acetate to 2-*methoxy*-3 : 4-*methylenedioxybenzaldehyde* (VI), which also has been synthesised.

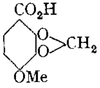
SOME years ago Penfold and Morrison (*J. Proc. Roy. Soc., N.S.W.*, 1923, **56**, 227) separated from the leaves and terminal branchlets of *Eriostemon crowei* (*Crowei saligna*) an essential oil the main constituent of which was a phenolic ether, croweacin, $C_{10}H_9O_2(OMe)$. This ether gave on oxidation with potassium permanganate a neutral product, now known to be a glycol, $C_{11}H_{14}O_5$, m. p. 97°, and an acid, croweacic acid, $C_9H_8O_6$, m. p. 153°. A consideration of these results suggested that the acid was a methoxymethylenedioxybenzoic acid isomeric with myristicic acid (5-methoxy-3 : 4-methylenedioxybenzoic acid) (I). This view was confirmed by the bromination of the acid: like myristicic acid, it gave 1 : 5 : 6-tribromo-2-methoxy-3 : 4-methylenedioxybenzene. It followed, therefore, that croweacic acid must be either 2-methoxy-3 : 4-methylenedioxybenzoic acid (II) or 4-methoxy-2 : 3-methylenedioxybenzoic acid (III). Synthesis has shown the former of these alternatives to be correct.




(I.)



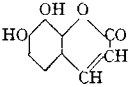

(II.)




(III.)

By the methylenation of methyl 2 : 3-dihydroxy-4-methoxybenzoate (Herzig and Pollak, *Monatsh.*, 1902, **23**, 707; 1904, **25**, 506) an *ester* was obtained which on hydrolysis gave 4-*methoxy*-2 : 3-*methylenedioxybenzoic acid* (III), m. p. 256°, different from croweacic acid.

Considerable difficulty was encountered in synthesising (II). Attempts to methylenate pyrogallol, its monoacetyl derivative, and methyl 2 : 3 : 4-trihydroxybenzoate with methylene sulphate or methylene iodide failed, a somewhat unexpected result in view of the ease with which the ester yields a dimethyl ether. Success was finally achieved by using daphnetin (IV) as the starting material. The phenol, obtained in poor yield by the facile method of v. Pechmann (*Ber.*, 1884, **17**, 929), gave on treatment with methylene sulphate *daphnetin methylene ether*, m. p. 188°, from which by methylation with methyl sulphate in alkaline solution α-2-*methoxy*-3 : 4-*methylenedioxycinnamic acid* (V), m. p. 131°, was prepared. This acid on ozonolysis in sodium carbonate solution gave 2-*methoxy*-3 : 4-

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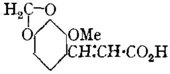


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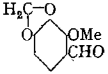


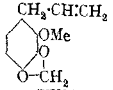

(VI.)

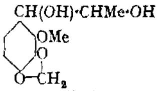
*methylenedioxybenzaldehyde* (VI), m. p. 104°, which was unaffected by an excess of ozone. Oxidation of the aldehyde with potassium permanganate in water–acetone solution gave 2-*methoxy*-3 : 4-*methylenedioxybenzoic acid* (II), identical in all respects with croweacic acid. The low melting point (131°) of the substituted cinnamic acid was somewhat unexpected and this acid probably represents the *cis*-modification, since an isomeric β-*form*, m. p. 212—213°, was prepared by the condensation of the aldehyde (VI) with malonic acid.

The structure of croweacic acid being established, it followed that croweacin must be either the propenyl ether (VII) or the allyl isomer (VIII). Unlike the closely related ethers myristicin and eugenol, croweacin must be represented by (VII); the glycol obtained

from it on oxidation with potassium permanganate is (IX), since it yields on further degradation with lead tetra-acetate an aldehyde, *m. p.* 104°, identical with 2-methoxy-3 : 4-methylenedioxybenzaldehyde (VI).

(VII.)


(VIII.)


(IX.)

## Experimental.

*Oxidation of Croweacin.*—Croweacin (1·8 g.; b. p. 129—131°/10 mm., $d_{15°}^{15°}$ 1·1324, $n_D^{20°}$ 1·5339) in pure acetone (20 c.c.) was treated with finely powdered potassium permanganate (5 g.) in portions with shaking and cooling in water. The manganese dioxide sludge was collected, washed with acetone, suspended in water, and dissolved by passage of sulphur dioxide. The solution was extracted with ether, the extract washed with water and dried, and the solvent removed. The residue, which solidified, was crystallised from dilute alcohol (1 : 1), croweacic acid (0·5 g.) separating in fine needles, m. p. 153° [Found : C, 55·0; H, 4·1; OMe, 16·1. Calc. for $C_8H_5O_4(OMe)$ : C, 55·1; H, 4·1; OMe, 15·8%]. The acetone filtrate was evaporated; the residue (0·2 g.) solidified on keeping. The glycol crystallised from ligroin (b. p. 100—120°) in needles, m. p. 97°.

*2-Methoxy-3 : 4-methylenedioxybenzaldehyde.*—The glycol (0·2 g.) and lead tetra-acetate in acetic acid (2·81N/50, 10 c.c.) were kept for 10 days, water then added, and the solution extracted with ether. After being washed with sodium carbonate solution, the extract was dried, and the solvent removed; the residue solidified. The *aldehyde* crystallised from hot water in fine long needles, m. p. 104°, both alone and in admixture with a synthetic specimen (Found : C, 60·3; H, 4·6. $C_9H_8O_4$ requires C, 60·0; H, 4·4%). The semicarbazone was identical with the synthetic specimen described on p. 758.

*Dibromocroweacin Dibromide.*—Bromine (1 c.c.) was added to croweacin (0·3 g.) in acetic acid (5 c.c.), and the solution kept for 12 hours prior to dilution with water. The precipitated solid was filtered off from much oily impurity, which did not solidify. The *dibromocroweacin dibromide* crystallised from dilute alcohol in fine needles, m. p. 108° (Found : C, 26·1; H, 2·2; Br, 62·4. $C_{11}H_{10}O_3Br_4$ requires C, 25·9; H, 2·0; Br, 62·7%).

1 : 5 : 6-*Tribromo-2-methoxy-3 : 4-methylenedioxybenzene.*—(i) Croweacic acid (and the synthetic acid) or 4-methoxy-2 : 3-methylenedioxybenzoic acid (0·2 g.), prepared as described below, and bromine (1 g.) were heated for 1 hour on the water-bath, early elimination of carbon dioxide occurring smoothly. Water was added and the precipitated solid was collected, washed with warm sodium carbonate solution, and crystallised from alcohol, the bromo-derivative separating in long needles, m. p. 157° (Found : C, 24·6; H, 1·4. Calc. for $C_8H_5O_3Br_3$ : C, 24·6; H, 1·3%). (ii) When myristicic acid (5-methoxy-3 : 4-methylenedioxybenzoic acid) was used, the above treatment failed to remove the carboxyl group, but the same neutral product, m. p. 157°, resulted when the heating was continued for 4 hours.

*Methyl 2 : 3 : 4-Trihydroxybenzoate.*—Pyrogallol (50 g.) by Kostanecki's method (*Ber.*, 1885, **18**, 3205) gave 2 : 3 : 4-trihydroxybenzoic acid (30 g.), which was refluxed with methyl-alcoholic hydrogen chloride (250 c.c.) for 8 hours. Most of the alcohol was distilled and the ester was then taken up in ether and distilled, giving an oil (25 g.), b. p. 182—184°/14 mm., which quickly solidified. Methyl 2 : 3 : 4-trihydroxybenzoate crystallised from water or dilute methyl alcohol in long needles, m. p. 148°, with considerable softening after air-drying (Found : C, 43·5; H, 5·5. Calc. for $C_8H_8O_5,2H_2O$ : C, 43·6; H, 5·4%). Will (*Ber.*, 1888, **21**, 2023) records results agreeing for $C_8H_8O_5,2{\cdot}5\ H_2O$. The anhydrous ester, m. p. 153°, was obtained by heating the hydrate at 100° under reduced pressure, the ester showing a slight tendency to sublime (Found : C, 52·2; H, 4·4. Calc.: C, 52·2; H, 4·3%).

2 : 3-*Dihydroxy-4-methoxybenzoic Acid.*—Anhydrous methyl 2 : 3 : 4-trihydroxybenzoate (25 g.) in ether was cooled in ice-water, and an ethereal solution of diazomethane (from nitrosomethylurea, 16 g.) slowly added. After removal of the ether, the ester, which failed to crystallise, was hydrolysed by alcoholic potassium hydroxide solution, giving a mixture of acids, separable by fractional crystallisation from water. 2-Hydroxy-3 : 4-dimethoxybenzoic acid (2·0 g.) separated first in long prisms, m. p. 170°, followed by fractions (6 g.), m. p. about 200°, which, when repeatedly crystallised, gave needles, m. p. 222° (Will, *loc. cit.*, gives m. p.

204—206°) (Found : C, 52·5; H, 4·5. Calc. for $C_8H_8O_5$ : C, 52·3; H, 4·3%). On esterification with methyl-alcoholic hydrogen chloride the highly crystalline methyl ester, m. p. 101°, was obtained, which on hydrolysis regenerated the acid, m. p. 222°.

*4-Methoxy-2 : 3-methylenedioxybenzoic Acid.*—Methylene sulphate (1·5 g.) was added in portions to the above ester (1·2 g.), potassium hydroxide (1 g.), water (10 c.c.), and acetone (10 c.c.), and the solution warmed until it became acid to litmus. The acetone was distilled off; on addition of water *methyl 4-methoxy-2 : 3-methylenedioxybenzoate* (0·8 g.) separated, which crystallised from dilute alcohol or water in needles, m. p. 122—123° (Found : C, 57·2; H, 4·9. $C_{10}H_{10}O_5$ requires C, 57·1; H, 4·8%). The ester gave no colour with ferric chloride and was hydrolysed by aqueous sodium hydroxide solution (8%), the solntion on acidification giving *4-methoxy-2 : 3-methylenedioxybenzoic acid*, which crystallised from dilute alcohol in needles, m. p. 256° (Fonnd : C, 55·4; H, 4·4. $C_9H_8O_5$ requires C, 55·1; H, 4·1%).

*Daphnetin Methylene Ether.*—To a solution of daphnetin (2 g.) in potassium hydroxide (2 g.), water (20 c.c.), and acetone (20 c.c.), warmed on the water-bath, methylene sulphate (3 g.) was added in portions, the red colonr of the solution gradually changing to brown. From the product of three similar experiments the acetone was removed, and water added; on cooling, a crystalline solid quickly separated. This was immediately filtered off and treated with sodium carbonate solution to remove unchanged daphnetin. The resulting *daphnetin methylene ether* (1·6 g.) crystallised from alcohol in plates, m. p. 188° (Found : C, 63·0; H, 3·3. $C_{10}H_6O_4$ requires C, 63·2; H, 3·1%). From the acidified mother-liquors, unchanged daphnetin (3·5 g.) was obtained.

*α-2-Methoxy-3 : 4-methylenedioxycinnamic Acid.*—Daphnetin methylene ether (1 g.) was heated on the water-bath with sodium hydroxide solution (10 c.c., 20%) and to the clear solution methyl sulphate (8 g.) was added with shaking until clouding occurred owing to the separation of the methyl ester. A similar further quantity of sodium hydroxide solution was added, and the mixture heated on the water-bath until a clear solution was obtained. This was cooled and acidified, the precipitated solid collected and treated with sodium carbonate solution, a little unchanged daphnetin methylene ether filtered off, and the filtrate acidified. The *cinnamic acid* (0·8 g.) crystallised from dilute alcohol (1 : 1) in long needles, m. p. 131° (Found : C, 59·3; H, 4·5. $C_{11}H_{10}O_5$ requires C, 59·5; H, 4·5%).

*2-Methoxy-3 : 4-methylenedioxybenzaldehyde.*—The cinnamic acid (1 g.) was dissolved in aqueous sodium carbonate (10 c.c., 8%), and ozone passed through the solution for 4 hours, as it was not completely absorbed. A white precipitate, which gradually separated, was collected on completion of the oxidation. The *aldehyde* (0·6 g.) crystallised from water in long fine needles, m. p. 104° (Found : C, 60·1; H, 4·4. $C_9H_8O_4$ requires C, 60·0; H, 4·4%). The *semicarbazone*, prepared in aqueous solution, crystallised from alcohol, in which it was somewhat sparingly soluble, in hair-like needles, m. p. 238° (Found : N, 17·1. $C_{10}H_{11}O_4N_3$ requires N, 17·7%). The *2 : 4-dinitrophenylhydrazone* crystallised from ethyl acetate in red needles, m. p. 254° (Found : N, 15·5. $C_{15}H_{12}O_7N_4$ requires N, 15·6%).

*2-Methoxy-3 : 4-methylenedioxybenzoic Acid.*—The aldehyde (0·25 g.) in acetone (10 c.c.) was maintained at 40° while aqueous potassium permanganate (6 c.c., 3%) was added slowly. When the purple colour was discharged, the acetone was removed in a current of air, water (5 c.c.) added, and sulphur dioxide passed through the mixture to remove the manganese dioxide. The precipitated solid was collected and digested with sodium carbonate solution, and the unchanged aldehyde (0·1 g.) removed. *2-Methoxy-3 : 4-methylenedioxybenzoic acid* (0·15 g.) was precipitated on acidification of the sodium carbonate filtrate; it crystallised from water in needles, m. p. 153°, both alone and in admixture with croweacic acid (Found : C, 55·1; H, 4·2. $C_9H_8O_5$ requires C, 55·1; H, 4·1%).

*β-2-Methoxy-3 : 4-methylenedioxycinnamic Acid.*—2-Methoxy-3 : 4-methylenedioxybenzaldehyde (0·2 g.), malonic acid (0·3 g.), pyridine (2 c.c.), and piperidine (1 drop) were heated for 2 hours on the water-bath. An excess of dilute hydrochloric acid precipitated the *β-cinnamic acid*, which crystallised from alcohol in needles, m. p. 212—213° (Found : C, 59·2; H, 4·6. $C_{11}H_{10}O_5$ requires C, 59·5; H, 4·5%).

We are indebted to the Government Grants Committee of the Royal Society and to Imperial Chemical Industries, Limited, for grants, and to Dr. T. A. Henry for the gift of a specimen of myristicic acid.

TECHNOLOGICAL MUSEUM, SYDNEY, NEW SOUTH WALES.
UNIVERSITY COLLEGE OF NORTH WALES, BANGOR. [*Received, April 4th*, 1938.]

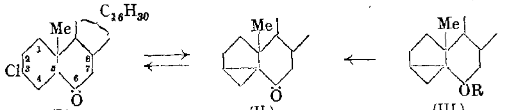
# 143. *Studies in the Sterol Group. Part XXXVI. The Oxidation of* i-*Cholesterol and its Derivatives.*

By I. M. Heilbron, J. Hodges, and F. S. Spring.

Oxidation of *i*-cholesterol, *i*-cholesteryl acetate and *i*-cholesteryl methyl ether gives " heterocholestenone " in good yield. An examination of this ketone reveals that it does not contain an ethylenic linkage and that on treatment with dilute hydrochloric acid it is converted into α-3-chloro-6-ketocholestane. These observations in conjunction with the fact that " heterocholestenone " is readily obtained from the chloro-ketone show that the former is to be represented by (II). *i*-Cholesterol is therefore (III; R = H), a structure originally suggested by Wallis, Fernholz, and Gephart. The ketone obtained indirectly from *i*-cholesterol by Ford, Chakravorty, and Wallis cannot be homogeneous or alternatively it cannot have the structure (II) ascribed to it by these authors. Reduction of " heterocholestenone " with aluminium *iso*propoxide gives an alcohol, characterised as its acetate, m. p. 60°, which may be an epimer of *i*-cholesteryl acetate; the reaction is being further investigated.

The oxidation of *i*-cholesterol was studied by Wallis, Fernholz, and Gephart (*J. Amer. Chem. Soc.*, 1937, **59**, 137), who isolated from the neutral fraction a solid product of unsharp melting point, from which they obtained an oxime, m. p. 143—144°. Ford, Chakravorty, and Wallis (*J. Amer. Chem. Soc.*, 1938, **60**, 413) showed that on hydrolysis by means of alcoholic sulphuric acid, the oxime gave a ketone, m. p. 110—111°, which on treatment with hydrogen chloride in acetic acid yielded α-3-chloro-6-ketocholestane (I). Prior to the appearance of the memoir of Ford, Chakravorty, and Wallis we also had effected the conversion of *i*-cholesterol and its derivatives into α-3-chloro-6-ketocholestane and we now report upon our results because there are certain marked differences in the intermediates isolated by us and by the American authors.

In our hands the oxidation of either *i*-cholesterol, *i*-cholesteryl acetate or *i*-cholesteryl methyl ether with chromic acid at room temperature * gives a ketone, $C_{27}H_{44}O$, m. p. 97°, $[\alpha]_D^{18°}$ + 40·9°, identical with the " heterocholestenone " prepared by Windaus and Dalmer (*Ber.*, 1919, **52**, 168) by treatment of α-3-chloro-6-ketocholestane (I) with alcoholic potassium hydroxide solution or alternatively by sublimation of the chloro-ketone (Windaus and Staden, *Ber.*, 1921, **54**, 1059). Windaus and Dalmer clearly considered the ketone to be unsaturated and this belief was substantiated by its catalytic hydrogenation to 6-ketocholestane. We find that " heterocholestenone " exhibits an absorption spectrum indicative of an isolated carbonyl group and therefore it cannot be 6-keto-$\Delta^4$-cholestene. Moreover it fails to react with perbenzoic acid and gives no coloration with tetranitromethane in chloroform solution. Furthermore on treatment with hydrochloric acid in acetic acid " heterocholestenone " is quantitatively converted into α-3-chloro-6-ketocholestane (I), a reaction similar to that exhibited by *i*-cholesterol and its derivatives




(I.) (II.) (III.)

with the same reagent (Beynon, Heilbron, and Spring, J., 1936, 907; 1937, 1459). " Heterocholestenone " therefore contains a bridge ring and not an ethylenic linkage and must have the structure (II); the ketone, m. p. 110—111°, described by Ford, Chakravorty, and Wallis is either not homogeneous or it cannot have the structure (II) ascribed to it by these authors. The conversion of *i*-cholesterol and its derivatives into " heterocholestenone " has thus been effected without rupture of the bridge ring system. The

* Oxidation of *i*-cholesteryl methyl ether in acetic acid at 97° gives 7-ketocholesteryl acetate as the sole neutral product.

formation of "heterocholestenone" from *i*-cholesterol clearly indicates that the latter is hydroxylated at $C_6$ and that it is to be represented by (III, R = H), a structure originally suggested by Wallis, Fernholz, and Gephart (*loc. cit.*). With the object of confirming this structure, the reduction of "heterocholestenone" with aluminium *iso*propoxide has been investigated. The product, however, was an oily alcohol, characterised by its *acetate*, $C_{29}H_{48}O_2$, m. p. 60°, which is not identical with *i*-cholesteryl acetate. The acetate, m. p. 60°, and its parent alcohol, like *i*-cholesteryl acetate and *i*-cholesterol, readily react with dilute hydrochloric acid to give cholesteryl chloride. It is possible that the acetate, m. p. 60°, is an epimer of *i*-cholesteryl acetate and with this in mind the reduction of "heterocholestenone" is being further investigated.

## EXPERIMENTAL.

*Oxidation of* i-*Cholesterol: "Heterocholestenone."*—*i*-Cholesterol was oxidised with chromic acid at room temperature under the conditions used by Wallis, Fernholz, and Gephart (*loc. cit.*). The neutral fraction readily solidified on trituration with methyl alcohol and after repeated crystallisation from acetone, or more readily by sublimation in a vacuum, followed by crystallisation from acetone, gave "heterocholestenone" as needles, m. p. 97°, $[\alpha]_D^{18°}$ + 40·9° ($l$ = 1, $c$ = 2·3 in chloroform), showing no depression on admixture with an authentic specimen (Found: C, 84·1; H, 11·35. Calc. for $C_{27}H_{44}O$: C, 84·3; H, 11·5%). The *oxime* separated from methyl alcohol in colourless prisms, m. p. 123°, identical with that prepared from an authentic specimen of "heterocholestenone" (Found: C, 81·3; H, 11·2. $C_{27}H_{45}ON$ requires C, 81·1; H, 11·4%). "Heterocholestenone" was likewise obtained by the oxidation of *i*-cholesteryl acetate under exactly the same conditions, whereas the oxidation of *i*-cholesteryl methyl ether proceeded more slowly (48 hours).

α-3-*Chloro-6-ketocholestane from "Heterocholestenone."*—"Heterocholestenone" (0·1 g.) in glacial acetic acid (20 c.c.) and concentrated hydrochloric acid (1 c.c.) was kept overnight at room temperature. The reaction mixture was diluted with water and extracted with ether, and the extract washed with water and dried (sodium sulphate). The residue obtained on removal of the solvent was crystallised from methyl alcohol, giving α-3-chloro-6-ketocholestane in fine white needles, m. p. 131°, unchanged on admixture with an authentic specimen (Found: C, 76·7; H, 10·6. Calc. for $C_{27}H_{45}OCl$: C, 77·0; H, 10·8%).

*Reduction of "Heterocholestenone."*—The ketone (1·5 g.) was heated under reflux with aluminium *iso*propoxide (5 g.) in dry *iso*propyl alcohol (30 c.c.) for 48 hours. The alcohol was removed by distillation under reduced pressure, the residue treated with aqueous sodium hydroxide (10%), and the mixture extracted with ether. Removal of the solvent yielded an oil which would not crystallise. The oil was heated under reflux with an excess of acetic anhydride for 2 hours, the acetic anhydride removed under reduced pressure, and the residue taken up in alcohol. After standing at 0°, the *acetate* crystallised and after several recrystallisations from alcohol yielded hard white rosettes of needles, m. p. 60°, $[\alpha]_D^{18°}$ + 82·4° ($l$ = 1; $c$ = 1·5 in chloroform) (Found: C, 81·4; H, 11·3. $C_{29}H_{48}O_2$ requires C, 81·2; H, 11·3%).

*Cholesteryl Chloride from the Acetate, m. p. 60°, and its Parent Alcohol.*—The acetate or the oily alcohol (0·1 g.) in a mixture of glacial acetic acid (10 c.c.) and hydrochloric acid (0·5 c.c.) was set aside overnight. The crystalline mass was collected and recrystallised from alcohol, giving cholesteryl chloride in plates, m. p. 96°, unchanged on admixture with an authentic specimen.

7-*Ketocholesteryl Acetate from* i-*Cholesteryl Methyl Ether.*—*i*-Cholesteryl methyl ether (7 g.) in glacial acetic acid (300 c.c.) was treated with chromic acid (15·4 g.) in 80% acetic acid solution (60 c.c.), added during 40 minutes with vigorous agitation, the temperature being maintained at 97° throughout. The mixture was cooled, largely diluted with water, and extracted with ether. The extract was washed repeatedly with aqueous sodium carbonate solution and dried (sodium sulphate). The oily product remaining after removal of the ether was triturated with methyl alcohol, and the solid (1·5 g.) crystallised from methyl alcohol, from which 7-ketocholesteryl acetate separated in needles, m. p. 157°, unchanged on admixture with an authentic specimen.

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THE UNIVERSITY, MANCHESTER. [*Received, April 5th, 1938.*]

# 144. *Complex Formation between Polynitro-compounds and Aromatic Hydrocarbons. Part IV. The Interaction of Trinitromesitylene and Trichlorotrinitrobenzene with Hexamethylbenzene and with Naphthalene.*

By D. Ll. Hammick and A. Hellicar.

Trichlorotrinitrobenzene forms solid complexes and coloured liquid phases with hexamethylbenzene and with naphthalene; trinitromesitylene does not. The sizes of the methyl group and of the chlorine atom being nearly the same and their mesomeric effects being in the same sense, it is concluded that the inhibiting effect of the methyl group is connected with its positive (electron-repelling) inductive effect, which is opposite to that of the electron-attracting chlorine atom. The bearing of these conclusions on the question of the structure of the complexes is discussed.

The solid compounds of trinitrotoluene with aromatic hydrocarbons are less stable than those of trinitrobenzene. The effect of methyl groups on the stability of these complexes is still more marked when a second such group is introduced. For instance, Efremov and Tikhomirova (*Ann. Inst. Anal. Phys. Chim. Leningrad*, 1928, **4**, 92) were unable to obtain solid compounds of trinitro-*m*-xylene with any of a large number of aromatic hydrocarbons.

In order to obtain further insight into the mechanism of this inhibiting effect of the methyl group, we have looked for evidence of intermolecular-compound formation in the two-component systems containing (*a*) trinitromesitylene and (*b*) trichlorotrinitrobenzene with, in each case, hexamethylbenzene or naphthalene. The nitro-compounds were chosen so as (*a*) to eliminate any effect on compound formation due to the presence in the molecules of nuclear hydrogen, and (*b*) to keep the steric effect of the substituent groups as nearly as possible the same, the screening effects of the chlorine atom and the methyl group being very nearly equal.* The mesomeric effect they exert on the benzene nucleus is in each case in the same sense ($+M$); but the methyl group by its inductive effect ($+I$) repels electrons, whereas the chlorine atom ($-I$) attracts them. We therefore expected to be able to compare the effect on the stability of the intermolecular complexes of the reversal of the sign of the inductive effect exerted on the nitro-groups by the other nuclear substituents.

Hexamethylbenzene was chosen as one of the aromatic hydrocarbons in order to have under examination nitro-compound–hydrocarbon systems containing no nuclear hydrogen at all.

Our experimental procedure has been to study solid–liquid equilibria in the various two-component systems. Our results, given in detail below, show that no solid complexes are stable in the trinitromesitylene systems, but that each of the hydrocarbons studied forms a solid complex with trichlorotrinitrobenzene. Moreover, the liquid phases in the trinitromesitylene and trichlorotrinitrobenzene systems are colourless and yellow respectively.

## Experimental.

Temperatures of solid–liquid equilibrium in the various systems were determined by the synthetic method. Weighed amounts of the two components were sealed up in weighed bulb-tubes, which were shaken in a variable thermostat until a (mean) temperature $T^{\circ}$ was found at which a small crystal of solid phase remained unchanged. Data are given below and plotted in the figure.

*Trinitromesitylene* (T.N.M.)–*Hexamethylbenzene* (H.M.B.).

| Mol.-fractn. H.M.B. | 0·00 | 0·09 | 0·18 | 0·27 | 0·40 | 0·50 | 0·60 | 0·67 |
|---|---|---|---|---|---|---|---|---|
| $T$ | 232·0° | 231·0° | 226·2° | 220·2° | 211·7° | 205·0° | 196·1° | 187·5° |
| Solid phase | T.N.M. | | | | | | | |

| Mol.-fractn. H.M.B. | 0·70 | 0·74 | 0·80 | 0·86 | 0·90 | 1·00 |
|---|---|---|---|---|---|---|
| $T$ | 185·0° | 180·0° | 169·3° | 158·4° | 159·0° | 165·0° |
| Solid phase | T.N.M. | | | | H.M.B. | |

* The radius of the chlorine atom being taken as 0·99 A. and the radius of revolution of the C–H link in the methyl group as 1·09 A., a scale diagram (for which we are indebted to Mr. M. W. Lister) shows that the surface of the chlorine atom would be 0·07 A. nearer than the sphere of revolution of the methyl group to an atom or group on the benzene nucleus between them.

*Trinitromesitylene* (T.N.M.)–*Naphthalene* (N.).

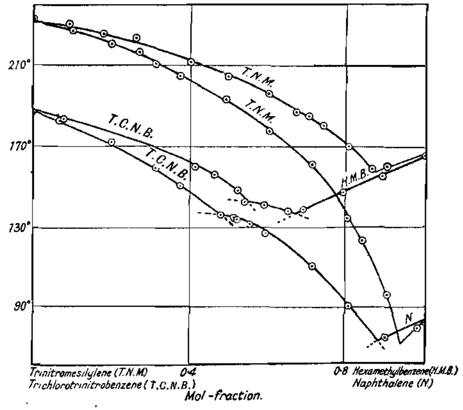
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Mol.-fractn. N. | 0·0 | 0·10 | 0·20 | 0·27 | 0·37 | 0·49 | 0·60 |
| *T* | 232·0° | 229·0° | 220·7° | 216·5° | 205·2° | 192·5° | 177·0° |
| Solid phase | T.N.M. | | | | | | |
| Mol.-fractn. N. | 0·71 | 0·80 | 0·84 | 0·90 | 0·98 | 1·00 | |
| *T* | 160·0° | 135·5° | 122·0° | 95·3° | 78·5° | 80·0° | |
| Solid phase | T.N.M. | | | | N. | | |

*Trichlorotrinitrobenzene* (T.C.N.B.)–*Hexamethylbenzene* (H.M.B.).

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Mol.-fractn. H.M.B. | 0·00 | 0·08 | 0·19 | 0·41 | 0·46 | 0·52 | |
| *T* | 187·0° | 183·2° | 175·0° | 159·5° | 155·0° | 146·9° | |
| Solid phase | T.C.N.B. | | | | | | |
| Mol.-fractn. H.M.B. | 0·54 | 0·59 | 0·65 | 0·69 | 0·79 | 0·89 | 1·00 |
| *T* | 141·5° | 140·0° | 137·5° | 138·1° | 146·5° | 154·5° | 165·0° |
| Solid phase | 2 : I Compound | | | H.M.B. | | | |

*Trichlorotrinitrobenzene* (T.C.N.B.)–*Naphthalene* (N.).

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Mol.-fractn. N. | 0·00 | 0·07 | 0·20 | 0·31 | 0·37 | 0·48 | | |
| *T* | 187·0° | 183·0° | 171·2° | 158·3° | 149·8° | 135·0° | | |
| Solid phase | T.C.N.B. | | | | | | | |
| Mol.-fractn. N. | 0·51 | 0·52 | 0·55 | 0·59 | 0·71 | 0·80 | 0·90 | 1·0 |
| *T* | 134·2° | 129·8° | 130·0° | 127·2° | 108·9° | 89·0° | 74·3° | 80·0° |
| Solid phase | 2 : I Compound | | | | | | N. | |



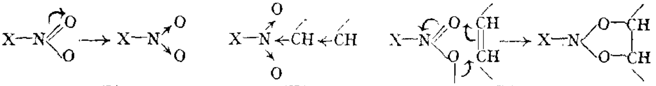

## Discussion of Results.

The temperature–composition curves in the figure indicate clearly the existence in the systems containing trichlorotrinitrobenzene of solid complexes with (probably) two molecules of nitro-compound to one of hydrocarbon. On the other hand, no indication is given of the stable existence of solid intermolecular compounds in the corresponding systems containing trinitromesitylene.

Whether or not a solid complex AB will separate from a liquid mixture containing A and B depends not only on the amount of AB present in the liquid phase but also on its solubility (Dimroth and Bamberger, *Annalen*, 1924, **438**, 67). Hence we cannot be quite sure that, because no solid compounds of trinitromesitylene with hexamethylbenzene and naphthalene exist, no chemical interaction takes place between the components in the

liquid phases. However, it may be noted that, of the two nitro-compounds, trichlorotrinitrobenzene has the lower melting point (187°) and is more soluble in organic solvents than trinitromesitylene (m. p. 232°). It would therefore not be unreasonable to expect that the hydrocarbon compounds of trinitromesitylene would be less soluble than those of trichlorotrinitrobenzene. The fact therefore that no solid compounds of trinitromesitylene were found points rather strongly to the conclusion that, even if there are any compound molecules present in the liquid phases, they must be relatively much less abundant than in the melts of trichlorotrinitrobenzene and the two hydrocarbons studied. Very strong support for this view comes from the observation that, whereas the trinitromesitylene–hydrocarbon melts are quite colourless, those containing trichlorotrinitrobenzene are bright yellow. (Molten trichlorotrinitrobenzene itself is almost colourless.)

As has been explained above, the steric effects of the substituents methyl and chlorine are very nearly the same, that of the latter being if anything the greater. The mesomeric effects of the methyl group and the chlorine atom being in the same sense, we therefore feel justified in concluding that the difference between the reactivities of the two nitro-compounds is connected with the fact that the inductive effect ($+I$) of the methyl group makes it electron-repelling whereas the chlorine atom ($-I$) is electron-attracting.



(I.) (II.) (III.)

According to Bennett and Willis (J., 1929, 256), the interaction of a nitro-group with an aromatic (ethylenic) substance involves the electromeric process (I) either before or during attack by or on an ethylenic bond in the polarised form —CH=CH— to give (II). The primary electromerism in the nitro-group should be facilitated by inductive effects in X tending to repel electrons from the nitrogen to the oxygen atoms. As pointed out above, methyl groups in the aromatic nucleus of X would be expected to do this, the influence of the chlorine atoms acting in the opposite direction. But we have found that the introduction of methyl groups into the trinitrobenzene molecule, far from increasing its readiness to interact with aromatic hydrocarbons, actually stops it altogether.

It has been suggested (J., 1935, 580) that the reactivity of the nitro-group may depend on the electromeric process (III). Such a process would be opposed by the presence of electron-repelling ($+I$) substituents in X, but should be facilitated, as is found to be the case, by electron-attracting ($-I$) substituents such as the chlorine atom. It will be noticed that on this view the effect of the chlorine atoms on the nitro-groups is the same as that of other electron-attracting substituents ($NO_2$, $SO_2Cl$, CN, etc.), without which a single nitro-group is ineffective (Bennett and Willis, *loc. cit.*; Bennett, *Ann. Reports*, 1931, **28**, 138; Bennett and Wain, J., 1936, 1108).

THE DYSON PERRINS LABORATORY, OXFORD. [*Received, March 23rd*, 1938.]

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# **145.** *Complex Formation between Polynitro-compounds and Aromatic Hydrocarbons. Part V. The Effect of Methylation on the Stability of Tetranitromethane Complexes.*

By T. T. DAVIES and D. LL. HAMMICK.

The colour density of mixtures of tetranitromethane in carbon tetrachloride with aromatic hydrocarbons increases as more hydrocarbon is added, and from measurements of the rate of increase of colour the relative stabilities of the coloured intermolecular complexes can be derived. In this way it is shown that stabilities increase

as the number of methyl groups attached to the benzene nucleus is increased to six. Introduction of methyl groups into the side chain of toluene, however, does not progressively increase the stability of the tetranitromethane complexes.

In Part III (J., 1936, 1463) it has been shown that the variation in colour density of a fixed volume of a solution of tetranitromethane with increase in the ratio of aromatic hydrocarbon to nitro-compound is proportional to the product $\varepsilon K$ of extinction coefficient and equilibrium constant for the interaction to form the coloured intermolecular complex. It was found that values of the product $\varepsilon K$ for a series of hydrocarbons were in the same order as the equilibrium constants for the interaction of the same hydrocarbons with picric acid (Moore, Shepherd, and Goodall, J., 1931, 1447; Dimroth and Bamberger, *Annalen*, 1924, **438**, 67). It was therefore concluded that the variation of $\varepsilon$ with the nature of the hydrocarbon is small and that the method might be used as a general method for comparing the stabilities of the coloured complexes formed by tetranitromethane with other aromatic and unsaturated substances.

In the present communication we give the results of an investigation of the effect of the progressive introduction of methyl groups into the benzene nucleus and into the side chain of toluene on the stability of the coloured complexes formed with tetranitromethane in carbon tetrachloride solution. We have included diphenyl- and triphenyl-methane among the hydrocarbons examined in order to make a comparison possible between the effect of the substitution of methyl and of phenyl into the toluene side chain on the stability of the complexes.

## Experimental.

*Materials.*—The tetranitromethane and carbon tetrachloride were prepared and purified as described in Part III (*loc. cit.*); the hydrocarbons were prepared by standard methods their purity being checked by determinations of b. p. and refractive index. We are indebted to Professor R. Robinson for a specimen of *tert.*-butylbenzene.

*Measurement of Colour Density.*—The experimental procedure was as described in Part III, progressively increasing quantities ($b$ g.-mols.) of hydrocarbon being added from a microburette to a fixed amount ($a$ g.-mols.) of tetranitromethane in carbon tetrachloride, the mixture being made up in each case to a standard volume $V$ (4 c.c.) with carbon tetrachloride. The colour density $D$ was determined in a Hilger–Nutting spectrophotometer fitted with a device for circulating a thermostatically controlled stream of water around the observation tube.

In Part III it was shown that $(\partial D/\partial b)_{a,V} = aK\varepsilon d/V^2$ * if the amount of coloured complex is relatively small. For fixed $a, V$, and $d$ (depth of absorbing solution), the colour-density slopes $(\partial D/\partial b)_{a,V}$ are proportional to $K$, the equilibrium constants [$K = c/(a - c)(b - c)$ where $c$ = no. of g.-mols. of coloured complex], if $\varepsilon$ does not vary much with the nature of the hydrocarbon. In the present communication we record the results of our measurements in a slightly different form. We have not kept to the same number of molecules of tetranitromethane in every case, and in order to make our results comparable, we have determined and compared the slopes

$$\left(\frac{\partial \frac{D}{a/V}}{\partial b/V}\right)_{a,V} = \frac{V^2}{a}\left(\frac{\partial D}{\partial b}\right)_{a,V} = K\varepsilon d$$

(The colour density–concentration of hydrocarbon slopes recorded in Part III are converted into the present units by division by 0·177.) As before, determinations of colour density were made at two temperatures ($T_1$ and $T_2$), and estimates made of the heats of interaction $H$ of tetranitromethane with the various hydrocarbons. Results are collected in Table I.

## Discussion.

The effect of the successive introduction of methyl groups into the benzene nucleus on the value of the product $K\varepsilon d$ at 25° is shown in Table II (*a*). The values of $K\varepsilon d$ for benzene, toluene, the xylenes, and mesitylene are taken from Part III (*loc. cit.*) and converted into the system of units used in the present communication.

* In Part III, this equation is given in error as $(\partial D/\partial b)_{a,}V = (a/V^2)(K/\varepsilon d)$.

TABLE I.

$V = 0{\cdot}004$ l.; values of $D$ found either directly at $\lambda = 4300$ A. or converted into $D_{4300}$ from sorption curves; $a/V$ and $b/V$ are the numbers of g.-mols. of tetranitromethane and of ydrocarbon per l. in the standard volume $V$ l. of carbon tetrachloride solution; $d$ was 2 cm. in l cases; $-\Delta H$ is the heat absorbed on formation of 1 g.-mol. of coloured complex assumed to e 1 : 1 in composition.

Durene. $T_1 = 25°$; $T_2 = 60°$; $a/V = 0{\cdot}419$ g.-mol./l.

| | | | | | | |
|---|---|---|---|---|---|---|
| $b/V$ | 0·0025 | 0·0050 | 0·9974 | 0·0124 | 0·0149 | 0·0248 |
| $D_{25°}$ | 0·304 | 0·499 | 0·653 | 1·136 | 1·380 | 2·35 |
| $D_{60°}$ | 0·231 | 0·432 | 0·557 | 0·940 | 1·112 | — |
| $D_{25°}/(a/V)$ | 0·73 | 1·19 | 1·56 | 2·71 | 3·29 | 5·61 |
| $D_{60°}/(a/V)$ | 0·55 | 1·02 | 1·33 | 2·24 | 2·66 | — |

$D_{25°}/a/V) = 226b/V + 0{\cdot}02$; $D_{60°}/(a/V) = 175b/V + 0{\cdot}02$; $-\Delta H = 1{\cdot}4$ kg.-cals./g.-mol.

Pentamethylbenzene. $T_1 = 25°$; $T_2 = 60°$; $a/V = 0{\cdot}423$ g.-mol./l.

| | | | | | | |
|---|---|---|---|---|---|---|
| $b/V$ | 0·0021 | 0·0042 | 0·0062 | 0·0083 | 0·0104 | 0·0125 |
| $D_{25°}$ | 0·289 | 0·575 | 0·782 | 1·114 | 1·412 | 1·596 |
| $D_{60°}$ | 0·230 | — | 0·665 | 0·831 | 1·099 | 1·243 |
| $D_{25°}/(a/V)$ | 0·684 | 1·360 | 1·850 | 2·635 | 3·340 | 3·777 |
| $D_{60°}/(a/V)$ | 0·544 | — | 1·573 | 1·966 | 2·601 | 2·941 |

$D_{25°}/(a/V) = 308b/V + 0{\cdot}03$; $D_{60°}/(a/V) = 233b/V + 0{\cdot}07$; $-\Delta H = 1{\cdot}7$ kg.-cals./g.-mol.

Hexamethylbenzene. $T_1 = 25°$; $T_2 = 60°$; $a/V = 0{\cdot}423$ g.-mol./l.

| | | | | | | |
|---|---|---|---|---|---|---|
| $b/V$ | 0·0019 | 0·0038 | 0·0057 | 0·0076 | 0·0095 | 0·0114 |
| $D_{25°}$ | 0·291 | 0·694 | 1·054 | 1·371 | 1·64 | 2·07 |
| $D_{60°}$ | 0·230 | 0·559 | 0·848 | 1·036 | 1·346 | 1·54 |
| $D_{25°}/(a/V)$ | 0·689 | 1·643 | 2·494 | 3·243 | 3·880 | 4·900 |
| $D_{60°}/(a/V)$ | 0·544 | 1·322 | 2·006 | 2·445 | 3·184 | 3·649 |

$D_{25°}/(a/V) = 430b/V + 0{\cdot}04$; $D_{60°}/(a/V) = 329b/V + 0{\cdot}04$; $-\Delta H = 1{\cdot}5$ kg.-cals./g.-mol.

Diphenylmethane. $T_1 = 25°$; $T_2 = 60°$ $a/V = 0{\cdot}4425$ g.-mol./l.

| | | | | | |
|---|---|---|---|---|---|
| $b/V$ | 0·051 | 0·102 | 0·203 | 0·254 | 0·305 |
| $D_{25°}$ | 0·236 | 0·458 | 0·854 | 1·068 | 1·312 |
| $D_{60°}$ | 0·216 | 0·399 | 0·730 | 0·963 | 1·158 |
| $D_{25°}/(a/V)$ | 0·533 | 1·035 | 1·931 | 2·413 | 2·966 |
| $D_{60°}/(a/V)$ | 0·488 | 0·902 | 1·650 | 2·176 | 2·622 |

$D_{25°}/(a/V) = 9{\cdot}52b/V + 0{\cdot}02$; $D_{60°}/(a/V) = 8{\cdot}65b/V + 0{\cdot}02$; $-\Delta H = 0{\cdot}5$ kg.-cal./g.-mol.

Triphenylmethane. $T_1 = 25°$; $T_2 = 60°$; $a/V = 0{\cdot}4125$ g.-mol./l.

| | | | | | | |
|---|---|---|---|---|---|---|
| $b/V$ | 0·0168 | 0·0338 | 0·0506 | 0·0675 | 0·0844 | 0·1161 |
| $D_{25°}$ | 0·184 | 0·353 | 0·498 | 0·689 | 0·851 | 1·161 |
| $D_{60°}$ | 0·172 | 0·323 | 0·454 | 0·602 | 0·757 | 1·050 |
| $D_{25°}/(a/V)$ | 0·446 | 0·857 | 1·208 | 1·671 | 2·065 | 2·817 |
| $D_{60°}/a/V$ | 0·417 | 0·784 | 1·102 | 1·461 | 1·837 | 2·548 |

$D_{25°}/(a/V) = 24{\cdot}25b/V + 0{\cdot}22$; $D_{60°}/(a/V) = 21{\cdot}53b/V + 0{\cdot}03$; $-\Delta H = 0{\cdot}66$ kg.-cal./g.-mol.

Ethylbenzene. $T_1 = 25°$; $T_2 = 60°$; $a/V = 0{\cdot}3540$ g.-mol./l.

| | | | | | |
|---|---|---|---|---|---|
| $b/V$ | 0·060 | 0·120 | 0·180 | 0·241 | 0·301 |
| $D_{25°}$ | 0·222 | 0·440 | 0·645 | 0·86 | 1·05 |
| $D_{60°}$ | 0·186 | 0·380 | 0·551 | 0·698 | 0·90 |
| $D_{25°}/(a/V)$ | 0·627 | 1·24 | 1·82 | 2·43 | 3·05 |
| $D_{60°}/(a/V)$ | 0·525 | 1·07 | 1·56 | 1·97 | 2·54 |

$D_{25°}/(a/V) = 10{\cdot}10b/V + 0{\cdot}01$; $D_{60°}/(a/V) = 8{\cdot}33b/V + 0{\cdot}04$; $-\Delta H = 1{\cdot}08$ kg.-cals./g.-mol.

*iso*Propylbenzene. $T_1 = 25°$; $T_2 = 60°$; $a/V = 0{\cdot}4125$ g.-mol./l.

| | | | | | | |
|---|---|---|---|---|---|---|
| $b/V$ | 0·0488 | 0·0975 | 0·1464 | 0·1972 | 0·2440 | 0·2928 |
| $D_{25°}$ | 0·159 | 0·300 | 0·430 | 0·549 | 0·713 | 0·861 |
| $D_{60°}$ | 0·145 | 0·252 | 0·355 | 0·456 | 0·619 | 0·698 |
| $D_{25°}/(a/V)$ | 0·386 | 0·728 | 1·041 | 1·332 | 1·730 | 2·088 |
| $D_{60°}/(a/V)$ | 0·352 | 0·611 | 0·902 | 1·109 | 1·502 | 1·693 |

$D_{25°}/(a/V) = 6{\cdot}97b/V + 0{\cdot}02$; $D_{60°}/(a/V) = 5{\cdot}68b/V + 0{\cdot}05$; $-\Delta H = 1{\cdot}15$ kg.-cals./g.-mol.

*tert.*-Butylbenzene. $T_1 = 25°$; $T_2 = 60°$; $a/V = 0{\cdot}3540$ g.-mol./l.

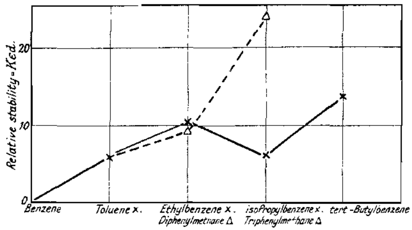
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| $b/V$ | 0·046 | 0·092 | 0·137 | 0·183 | 0·229 | 0·275 | 0·321 |
| $D_{25°}$ | 0·255 | 0·457 | 0·668 | 0·90 | 1·08 | 1·29 | 1·48 |
| $D_{60°}$ | 0·215 | 0·400 | 0·583 | 0·754 | 0·94 | 1·10 | 1·28 |
| $D_{25°}/(a/V)$ | 0·720 | 1·292 | 1·888 | 2·544 | 3·052 | 3·644 | 4·200 |
| $D_{60°}/(a/V)$ | 0·607 | 1·13 | 1·65 | 2·13 | 2·66 | 3·11 | 3·62 |

$D_{25°}/(a/V) = 13{\cdot}07b/V + 0{\cdot}07$; $D_{60°}/(a/V) = 10{\cdot}98b/V + 0{\cdot}10$; $-\Delta H = 0{\cdot}98$ kg.-cal./g.-mol.

TABLE II.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| (*a*) | $C_6H_6$ 0·4 | $C_6H_5Me$ 7·7 | $C_6H_4Me_2$ 55* | *s*-$C_6H_3Me_3$ 180 | 1 : 2 : 4 : 5-$C_6H_2Me_4$ 226 | $C_6HMe_5$ 308 | $C_6Me_6$ 430 |
| (*b*) | $C_6H_6$ 0·4 | $C_6H_5Me$ 7·7 | $C_6H_5Et$ 10·10 | $C_6H_5Pr^{\beta}$ 6·97 | $C_6H_5Bu^{\gamma}$ 13·07 | $CH_2Ph_2$ 9·52 | $CHPh_3$ 24·25 |

* Mean for *o*-, *m*-, and *p*-xylene.




If the reasons we have given for the view that ε does not vary much throughout the series are valid, it appears that the stability of the coloured complexes resulting from the interaction of tetranitromethane with these hydrocarbons increases steadily as the number of methyl groups increases.

The effect on stability of successive replacement by methyl groups of the side-chain hydrogens in toluene is, however, different. As is shown in Table II(*b*) and the figure, stability increases from benzene through toluene to ethylbenzene, falls with *iso*-propylbenzene and rises again at *tert.*-butylbenzene. On the other hand, each successive phenyl group introduced into the methyl group of toluene increases stability.

It is generally agreed that the part played by the hydrocarbon in forming complexes with polynitro-compounds is that of an anionoid reagent or electron donor. It therefore seem reasonable to connect the increased stability of the complexes of the methylated benzenes with the increase in anionoid reactivity that the nucleus might be expected to derive from successive replacements of hydrogen atoms by the electron-repelling (+ *I*) methyl groups. Replacement of the hydrogen atoms in the toluene side chain by successive methyl groups might *a priori* be expected to produce a similar though less marked effect. The drop in stability on passing from ethyl- to *iso*propyl-benzene implies therefore that the side-chain methylation of toluene not only increases the anionoid character of the nucleus but also has some other effect that lessens the stability of the tetranitromethane complexes. In other words, the anomalous effects of the substitution of methyl groups for alkyl hydrogen atoms observed in other fields (*e.g.*, Hughes and Ingold, J., 1935, 244; Baker and Nathan, *ibid.*, p. 1844) appear to be manifested on the decomposition side of the nitro-compound–aromatic hydrocarbon interaction. Further, in this connexion we may mention that analogous abnormalities in stability have been detected by preliminary experiments in the picric acid–aromatic hydrocarbon series.

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# 146. *The Constitutions of Eremophilone, Hydroxyeremophilone, and Hydroxydihydroeremophilone. Part II.*

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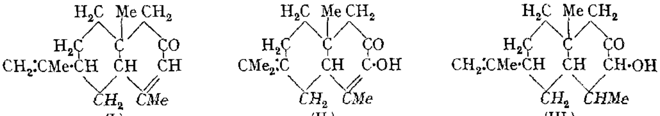
The observation (J., 1936, 667; 1937, 760) that tetrahydroeremophilone after treatment with methylmagnesium iodide and selenium dehydrogenation gave 1 : 5-dimethyl-7-*iso*propylnaphthalene and not 1 : 3-dimethyl-7-*iso*propylnaphthalene showed that the structure (I) could not correctly represent eremophilone. The difficulties involved by placing the carbonyl group of the ketone at position 5 are discussed and the conclusion is reached that, although dihydroeremophilol yields eudalene on selenium dehydrogenation, it cannot have an angle methyl group at position 9. An attempt has been made to determine the structure of hydroxyeremophilone, previously represented by (II), by a detailed investigation of its oxidation products and it is now found that one of these is a *keto-acid*, $C_{10}H_{16}O_3$. This suggested that the benzoate of hydroxyeremophilone might be (VII); the keto-acid would then be (IX). The latter acid should yield on reduction 2 : 2-dimethyl*cyclo*hexylacetic acid. Comparison with a synthetic specimen of this acid has shown this to be incorrect. The benzoate, therefore, cannot have the structure (VII) unless a molecular rearrangement has occurred during its degradation. Alternative formulæ for eremophilone and its congeners are discussed, but a final decision must await further experiments.

IT was suggested (Bradfield, Penfold, and Simonsen, J., 1932, 2744) that the three ketones, eremophilone, hydroxyeremophilone, and hydroxydihydroeremophilone, which occur together in the oil from the wood of *Eremophila Mitchelli*, were represented respectively by (I), (II), and (III). Before presenting the evidence which now leads us to reject these formulæ it is necessary to summarise briefly the grounds upon which they were based.



(I.) (II.) (III.)

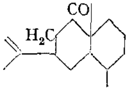
(A) *Eremophilone.* (i) The ketone contains two ethylenic linkages (catalytic hydrogenation). (ii) Dihydroeremophilol gives on selenium dehydrogenation eudalene and on ozonolysis formaldehyde and a keto-alcohol, $C_{14}H_{24}O_2$. From the latter a hydroxy-acid, $C_{13}H_{22}O_3$, was obtained by further oxidation with sodium hypobromite, thus proving conclusively the presence of an *iso*propenyl side chain in dihydroeremophilol. (iii) Eremophilone must contain the group $-$ $CH_2$·CO·CH:CH $-$. The presence of the methylene group was proved by the preparation of a crystalline hydroxymethylene derivative. Conjugation of the ethylene linkage with the carbonyl group was established (*a*) by the preparation of a compound with hydrogen sulphide, (*b*) by oxidation with hydrogen peroxide in alkaline solution to an oxide, eremophilone oxide (cf. Weitz and Scheffer, *Ber.*, 1921, **54**, 2327), and (*c*) the absorption spectrum (Gillam, J., 1936, 676).

(B) *Hydroxyeremophilone.* (i) The hydroxy-ketone can be prepared from eremophilone oxide. (ii) On ozonolysis it gives acetone with only a trace of formaldehyde, thus proving the presence of an *iso*propylidene group. (iii) Oxidation with hydrogen peroxide in alkaline solution yields, together with other products, two isomeric dibasic acids, $C_{15}H_{26}O_6$, suggesting the presence of a potential 1 : 2-diketone.

(C) *Hydroxydihydroeremophilone.* (i) The keto-alcohol gave on catalytic hydrogenation hydroxytetrahydroeremophilone, from which tetrahydroeremophilone was prepared by reduction with sodium amalgam, thus proving the relative positions of the hydroxyl and the carbonyl group. (ii) Ozonolysis gave formaldehyde (*iso*propenyl group), and with

hydrogen peroxide in alkaline solution one of the isomeric dibasic hydroxy-acids, $C_{15}H_{26}O_6$, previously prepared from hydroxyeremophilone, was obtained.

Recently, during the investigation of the structure of the sesquiterpene ketone, α-cyperone (J., 1936, 667; 1937, 760), we had occasion to investigate the action of methylmagnesium iodide on tetrahydroeremophilone and on selenium dehydrogenation of the product we obtained 1 : 5-dimethyl-7-*iso*propylnaphthalene in place of 1 : 3-dimethyl-7-*iso*propylnaphthalene. This showed, assuming no migration of the methyl groups at any stage, that in eremophilone the carbonyl group was in position 5, and not 3 as had been previously assumed. Evidence in support of this orientation was furnished by the fact that hydroxymethylene-eremophilone gave on reduction and dehydrogenation 1 : 6-dimethyl-7-*iso*propylnaphthalene. These experiments are satisfactorily accounted for only if we assign to eremophilone the skeleton structure (IV). Such a representation does not, however, permit of the conjugation of an ethylenic linkage with the carbonyl group, for which irrefutable evidence [see (A) above] has been provided. It became necessary, therefore, to subject the whole of the experimental evidence previously advanced to a critical revision, and a promising line of attack appeared to us to lie in a more detailed study of the degradation of hydroxyeremophilone.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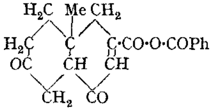
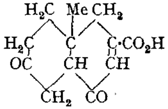

(V.)


(VI.)

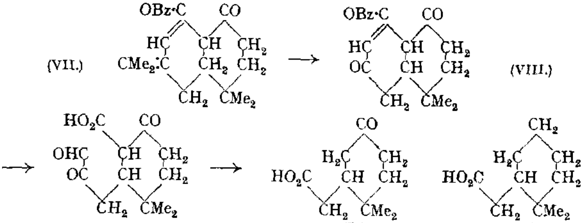
We recorded (*loc. cit.*, p. 2755) that when the benzoate of hydroxyeremophilone was ozonised it gave, in addition to acetone, a crystalline product, m. p. 186—188°, which we considered to have the composition $C_{19}H_{18}O_5$ and represented as the anhydride (V), since on digestion with alkali it gave benzoic acid and a keto-acid, analysed as the semicarbazone, m. p. 215—216°, and represented by (VI). It was, however, necessary to make the assumption that the semicarbazone crystallised with two molecules of alcohol of crystallisation.

We now find that the oxidation of the benzoate proceeds in a more complex manner than had been assumed and a further study of the products of this oxidation, together with the oxidation of hydroxyeremophilone and its methyl ether, has afforded a partial explanation of the fallacy underlying our previous conclusions.

When the benzoate is ozonised until the issuing gases just show the presence of ozone, the crystalline " anhydride " previously described, together with unchanged benzoate, can be readily isolated. As was mentioned (*loc. cit.*, p. 2755), this oxidation product is somewhat unstable and it tends to decompose on prolonged boiling with alcohol. It can be much more readily purified by crystallisation from ethyl acetate and analysis has shown that it contains two more hydrogen atoms than had been assumed previously and that it has the composition $C_{19}H_{20}O_5$. Its structure is discussed later (p. 769). If, however, the ozonolysis of the benzoate is prolonged, this crystalline product can no longer be isolated, the main product of the oxidation being a keto-acid, yielding the semicarbazone, m. p. 215—216°, referred to above. The analytical figures for carbon and hydrogen previously obtained have been confirmed, but a nitrogen estimation has shown that the semicarbazone has the composition $C_{11}H_{19}O_3N_3$. This composition is supported by hydrolysis of the semicarbazone to the parent *keto-acid*, $C_{10}H_{16}O_3$, m. p. 105—107°, an acid formed also in small amount when the " anhydride " is treated with alkali. This acid can be prepared by the oxidation of hydroxyeremophilone with chromic acid and by the ozonolysis of its methyl ether.

It is clearly very difficult to reconcile the formation of a keto-acid having this composition with the assignment to hydroxyeremophilone of a structure containing an angle methyl group in the 9-position, an assumption usually made in the case of sesquiterpene derivatives yielding eudalene on dehydrogenation. On the basis of the isoprene theory

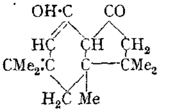
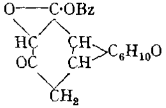
the most probable representation for the benzoate appeared to be (VIII); the keto-acid would then be (IX), the oxidation proceeding in accordance with the scheme:

(VII.)  (VIII.)

(IX.) (X.)

Reduction (Clemmensen) of the keto-acid gave a liquid acid, $C_{10}H_{18}O_2$, yielding a dextrorotatory p-*phenylphenacyl* ester, m. p. 65—67°, which, were the above reasoning correct, should be a derivative of *d*-2 : 2-dimethyl*cyclo*hexylacetic acid (X). This acid was therefore synthesised, but its *p*-phenylphenacyl ester (this vol., p. 776) was not identical with that prepared from the acid obtained by the degradation of the benzoate. The latter substance cannot therefore be represented by (VII) unless a wandering of a methyl group occurs during the Clemmensen reduction of the keto-acid (IX) or at some prior stage in the degradation.

An alternative structure for hydroxyeremophilone, also in accordance with the facts outlined above, is (XI), which contains three isoprene nuclei united in a somewhat unusual manner. Its conversion into eudalene on selenium dehydrogenation would involve the elimination of an angle methyl group, coupled with ring widening at the *gem*-dimethyl group.

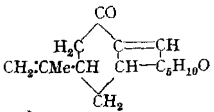
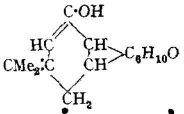
(XI.)   (XII.)

Our knowledge of the molecular rearrangements which may occur on selenium dehydrogenation is still limited (cf. Linstead, *Ann. Reports*, 1936, 294; Chatterjee, *J. Indian Chem. Soc.*, 1936, **13**, 588), so the possibility of this rearrangement cannot be rejected.

The structure of the crystalline "anhydride," m. p. 186—188°, has not been proved, but we suggest that it is the oxide (XII) formed by the action of hydrogen peroxide on the primary product (VIII) of the ozonolysis.

A further unusual product of the ozonolysis of the benzoate was an *acid*, $C_7H_6O_4$, m. p. 230—232°. This acid, which was comparatively stable and could be esterified with either diazomethane or methyl sulphate to give a liquid methyl ester yielding the original acid on alkaline hydrolysis, is probably a moloxide of benzoic acid, since it gives this acid in quantitative yield on sublimation in a low vacuum.

Although, therefore, the experiments outlined above have not enabled us to elucidate in their entirety the structures of eremophilone and hydroxyeremophilone, we think

(XIII.)   (XIV.)

that there can be no doubt that eremophilone and hydroxyeremophilone must contain the skeletons (XIII) and (XIV) respectively. In the latter formula the carbonyl group

of eremophilone is represented as enolising to give the hydroxy-group of hydroxyeremophilone. This is in accord with the complete conversion of the *iso*propenyl group in the former into an *iso*propylidene group in the latter occasioned by conjugation of the ethylenic linkages. We may note here also that any structure for hydroxydihydroeremophilone must permit of the enolisation of the carbonyl group, since the presence of two acetyl groups in the diacetate previously described (*loc. cit.*, p. 2757) has been confirmed by analysis. Furthermore, the ethylenic linkages in eremophilone cannot be conjugated, since the hydrocarbon, prepared from the semicarbazone of the ketone by the Wolff-Kishner reaction, cannot be reduced by sodium and alcohol.

It was mentioned above that when hydroxyeremophilone was oxidised with chromic acid the keto-acid $C_{10}H_{16}O_3$ was obtained. A further product of the oxidation is a *substance*, $C_{12}H_{18}O_3$, m. p. 193—194·5°, which has pseudo-acidic properties and has been characterised by the preparation of an *acetate*, m. p. 164—165°, and a *methyl* ether, m. p. 121—122°. The phenol gives no colour with ferric chloride and it does not appear to react with carbonyl reagents. We have obtained no clue to its structure, since it yields no recognisable degradation products. It is formed also by the ozonolysis of hydroxyeremophilone and its methyl ether.

We have reinvestigated the catalytic hydrogenation of hydroxyeremophilone benzoate (*loc. cit.*, p. 2757) and we now find that the product is not homogeneous. If the reduced benzoate is hydrolysed and the product distilled, an oil is obtained which partly crystallises. The solid, m. p. 89—90°, has the composition $C_{15}H_{24}O_2$ and it is therefore isomeric with hydroxydihydroeremophilone. It differs from this substance in giving an intense ferric chloride coloration and we suggest that it be designated β-*hydroxydihydroeremophilone*. It is probable that it still contains the enolic hydroxy-group present in hydroxyeremophilone, the exocyclic ethylenic linkage having been reduced. It is somewhat unstable, becoming gummy on keeping—a change which does not appear to be due solely to oxidation, since it proceeds also in the absence of air. It gives on oxidation with hydrogen peroxide in alkaline solution a liquid acid. The liquid from which β-hydroxydihydroeremophilone had been separated and which, from its colour with ferric chloride, still contained much of this substance, was oxidised with hydrogen peroxide in alkaline solution; it then gave a small quantity of a crystalline *acid*, $C_{15}H_{26}O_4$, m. p. 193—195°. A further product of the oxidation was a *phenolic oxide*, $C_{15}H_{24}O_3$, m. p. 136—137°.

During these experiments we have devised a more convenient method for the separation of eremophilone and hydroxyeremophilone and we have obtained evidence of the presence in the oil of a fourth ketone having the composition $C_{15}H_{22}O$. It is present in the lower-boiling fractions, but it could not be obtained free from eremophilone. It was characterised by the preparation of a 2 : 4-*dinitrophenylhydrazone*, m. p. 155—156·5°.

## Experimental.

*Separation of Eremophilone and Hydroxyeremophilone.*—The crude oil from *E. Mitchelli* (200 g.) was dissolved in pyridine (400 c.c.) and to the cooled solution benzoyl chloride (112 g.) was gradually added. After being kept overnight, the mixture was poured on ice and dilute sulphuric acid, the oil dissolved in ether, and the ethereal solution washed with dilute sulphuric acid, sodium hydroxide solution, and water, and dried. The viscid gum (280 g.) left on removal of the solvent was dissolved in ligroin (b. p. 40—60°) (500 c.c.) and, after inoculation with hydroxyeremophilone benzoate, kept in the ice-box for 48 hours. The benzoate (52 g.), which had separated, was collected, and the filtrate, after removal of the ligroin, distilled at 3 mm., two fractions being collected: (i) up to 190° and (ii) 190—250°.

Fraction (i) was dissolved in ether, washed with sodium carbonate solution to remove benzoic acid, dried, recovered (72 g.), and distilled, the main fraction having b. p. 170—180°/20 mm. This partly crystallised; the solid eremophilone was collected, and the filtrate repeatedly fractionated, the crystalline eremophilone which separated from the higher-boiling fractions being removed. Ultimately the following fractions (at 11 mm.) were obtained: (*a*) b. p. up to 140°; (*b*) 140—150°; (*c*) 160—163°, mainly 155—158°, and (*d*) 163—168°. Fraction (*d*) crystallised and consisted essentially of eremophilone. From fraction (*c*), which formed the main fraction of lower boiling point, and also from fraction (*b*), a 2 : 4-*dinitro-*

*phenylhydrazone* was prepared which crystallised from alcohol in fine yellow needles, m. p. 155—156·5° (Found: C, 63·3; H, 6·4. $C_{21}H_{26}O_4N_4$ requires C, 63·3; H, 6·5%). The ketone corresponding to this dinitrophenylhydrazone could not be completely freed from eremophilone, as was shown by the fact that all the fractions gave with hydrogen peroxide in the presence of alkali small amounts of eremophilone oxide (this may possibly provide a method for the separation of the two ketones). The ketone gave a gummy semicarbazone and attempts to regenerate it from its dinitrophenylhydrazone failed.

Fraction (ii) (see above) was dissolved in ether, washed with sodium carbonate solution to remove benzoic acid, recovered (110 g.), and dissolved in ligroin (b. p. 40—60°) (200 c.c.); on keeping, a further quantity of hydroxyeremophilone benzoate (19 g.) separated. The oil soluble in ligroin was not further examined, but it probably contained the benzoate of hydroxydihydroeremophilone.

*Hydrocarbon from Eremophilonesemicarbazone.*—The semicarbazone (6 g.) was heated with sodium ethoxide (alcohol, 10 c.c.; sodium, 0·75 g.) at 210° for 6 hours. The hydrocarbon (3 g. from 18 g. of the semicarbazone) had b. p. 130°/13 mm. On titration with perphthalic anhydride (Böhme, *Ber.*, 1937, **70**, 379) it showed the presence of two ethylenic linkages and the titration value was unchanged after attempted reduction with sodium and alcohol.

*Conversion of Hydroxymethylene-eremophilone into* 1 : 6-*Dimethyl*-7-iso*propylnaphthalene.*—The mixture of solid (2·3 g.) and oil (*ca.* 6 g.) from the preparation of hydroxymethylene-eremophilone in methyl alcohol (150 c.c.) was shaken in hydrogen at 3 atm. pressure in the presence of a palladium–norit catalyst. The absorption of hydrogen was slow and ceased after 1350 c.c. had been taken up (calc., 3000 c.c.). Methyl alcohol was removed from the filtered solution by distillation through a column, and the residue, after drying in ethereal solution, further reduced with alcohol (200 c.c.) and sodium (20 g.). The recovered oil (4·5 g.) was heated with selenium (7 g.) at 300° for 40 hours and then at 320° for 12 hours. The somewhat tarry product was extracted with ether, the extract washed with sodium hydroxide solution, and dried, and the ether removed. The oil obtained (1·3 g.) gave a small yield of a picrate, which after crystallisation from alcohol had m. p. 123—125° both alone and in admixture with 1 : 6-dimethyl-7-*iso*propylnaphthalene picrate.

*Hydroxyeremophilone.*—Hydroxyeremophilone, prepared by the hydrolysis of the benzoate with alcoholic potassium hydroxide, was purified by distillation under diminished pressure, followed by crystallisation from methyl alcohol. Unlike the specimen described previously (*loc. cit.*, p. 2755), it gave correct figures on analysis (Found: C, 76·9; H, 9·4. Calc. for $C_{15}H_{22}O_2$: C, 76·9; H, 9·4%). Numerous attempts were made to establish the presence of a carbonyl group in the hydroxy-compound itself, the benzoate, and the acetate, m. p. *ca.* 55°, *b. p.* 210—211°/25 *mm., but were all unsuccessful. With Brady's reagent an amorphous* precipitate slowly formed, which could not be crystallised. The benzoate did not react with methylmagnesium iodide.

*Hydroxyeremophilone Methyl Ether.*—The alcohol (14 g.) in acetone (100 c.c.) was treated with methyl sulphate (10 c.c.) and aqueous sodium hydroxide (20 c.c.; 30%), the solution being kept just alkaline (mechanical stirring). A deep red colour developed at first, changing gradually to a pale yellow. After being kept overnight, the mixture was heated on the water-bath for 1 hour, cooled, and diluted with water, and the oil, which separated, dissolved in ether. The ethereal extract was washed successively with sodium hydroxide solution, dilute sulphuric acid, and water, and dried, and the solvent removed. The *methyl* ether (14·5 g.) was a faintly yellow oil, b. p. 180°/13 mm. (Found: C, 77·4; H, 9·7. $C_{16}H_{24}O_2$ requires C, 77·4; H, 9·7%). Hydroxyeremophilone does not react with diazomethane. The methyl ether, which gave no colour with ferric chloride, could not be reduced with aluminium *iso*propoxide. On treatment with *iso*amyl formate in ethereal solution in the presence of sodium an oil, soluble in alkali, was obtained, which gave with alcoholic ferric chloride a deep red coloration. The oil reacted at once with carbonyl reagents, but the derivatives were amorphous. Amorphous products were obtained also by the interaction of the methyl ether with piperonal and *m*-nitrobenzaldehyde.

β-*Hydroxydihydroeremophilone.*—Hydroxyeremophilone benzoate (23 g.) in ethyl acetate was reduced under pressure (3 atm.) in the presence of a palladium–norit catalyst; absorption of hydrogen was very slow and ceased completely after slightly more than 1 mol. of hydrogen had been taken up. Removal of the solvent from the filtered solution left a viscid gum, which was hydrolysed with methyl-alcoholic potassium hydroxide solution; addition of water then precipitated an oil. This was isolated by ether in the usual manner; the residue (13 g.) remaining after removal of the solvent partly crystallised and had b. p. 169—172°/13 mm.

From the semi-solid distillate, which gave an intense green colour, changing to blue, with alcoholic ferric chloride, the solid was separated. *β-Hydroxydihydroeremophilone* crystallised from dilute methyl alcohol in slender prisms, m. p. 89—90°, $[\alpha]_{5461} + 42°$ in methyl alcohol (*c*, 2·07) (Found: C, 76·3; H, 10·1. $C_{15}H_{24}O_2$ requires C, 76·3; H, 10·2%). The solid gave the same colour reactions with ferric chloride as the oil.

The oil (6·5 g.), b. p. 165—167°/12 mm., from which the solid had been separated was dissolved in methyl alcohol (45 c.c.) and treated with a mixture of sodium hydroxide solution (4N; 12 c.c.) and hydrogen peroxide (11%; 31 c.c.). No heat was generated and after 1 hour the mixture was heated at 50°; a vigorous reaction then ensued, sufficient heat being generated to maintain this temperature for 30 minutes. After 12 hours water was added, the neutral oil (3 g.) removed by ether, and the solution acidified and extracted with ether. The ethereal extract was washed with sodium carbonate and then with sodium hydroxide solution. From the latter, carbon dioxide precipitated a *phenol*, which crystallised from dilute methyl alcohol in long prismatic needles, m. p. 136—137°, giving an olive-green ferric chloride coloration (Found: C, 71·5; H, 9·4. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·5%). From the sodium carbonate solution, an acid (4·5 g.) was isolated which partly crystallised on trituration with formic acid. The crystalline *acid* separated from methyl alcohol (50%) in soft needles, m. p. 193—195° (Found: C, 66·5; H, 9·4; *M*, 278. $C_{15}H_{26}O_4$ requires C, 66·7; H, 9·6%; *M*, 270). The acid appeared to be stable to potassium permanganate in alkaline solution and it gave with acetyl chloride a liquid anhydride.

*Oxidation of Hydroxyeremophilone and its Derivatives.*—(a) *Ozonolysis of hydroxyeremophilone.* The ketone (5 g.) in ethyl acetate (25 c.c.) was treated with ozone at 0° until the gas passed through freely. The solvent was removed from the deep yellow solution under diminished pressure and after the addition of water (10 c.c.) the ozonide was decomposed by heating on the water-bath for 1 hour. Sodium carbonate was added, the insoluble oil dissolved in ether, the ethereal extract washed with sodium hydroxide solution (B), and the solvent removed. The residue (0·4 g.) was unchanged hydroxyeremophilone. Acidification of the sodium hydroxide solution (B) precipitated a solid (1·2 g.), which crystallised from methyl alcohol (70%) in thin plates, m. p. 191—192°, both alone and after admixture with the phenol obtained from the oxidation of hydroxyeremophilone with chromic acid (see below). The identity was confirmed by the preparation of the acetyl derivative, m. p. 164—165°.

The sodium carbonate solution on acidification gave a gummy acid (3·2 g.). This reacted with carbonyl reagents to give amorphous products and on oxidation with sodium hypobromite gave a small amount of bromoform.

(b) *Oxidation of hydroxyeremophilone with chromic acid.* To a solution of the ketone (6·2 g.) in acetic acid (50 c.c.), chromic acid (7 g.) in acetic acid (40 c.c.) and water (10 c.c.) was added during 8 hours (mechanical stirring). After the addition of water (50 c.c.) the excess of chromic acid was removed by sulphur dioxide, and the greater part of the acetic acid distilled off with steam. The cooled residue from the steam distillation, after saturation with ammonium sulphate, was extracted with ether, and the extract washed with sodium hydroxide solution, dried, and evaporated, a small amount of hydroxyeremophilone being recovered. Saturation of the sodium hydroxide solution with carbon dioxide precipitated a phenol (1·2 g.), the filtrate (*A*) being reserved. The *phenol* crystallised from dilute methyl alcohol in thin plates or prisms, m. p. 193—194·5° (Found: C, 68·3; H, 8·4. $C_{12}H_{18}O_3$ requires C, 68·6; H, 8·6%). It gave in alkaline solution with sodium hypobromite an immediate precipitate of bromoform, but the acid product of the oxidation could not be characterised. The *acetyl* derivative, prepared by digestion of the phenol with acetic anhydride containing a trace of pyridine, crystallised from methyl alcohol in well-formed prisms m. p. 164—165° (Found: C, 66·7; H, 7·9. $C_{14}H_{20}O_4$ requires C, 66·7; H, 7·9%). The *methyl* ether, prepared by the action of methyl sulphate, crystallised from methyl alcohol in hexagonal prisms, m. p. 121—122° (Found: C, 69·3; H, 8·5. $C_{13}H_{20}O_3$ requires C, 69·6; H, 8·9%).

The sodium carbonate solution (*A* above), from which the phenol had been separated, was acidified and extracted with ether. The liquid residue remaining after removal of the solvent was triturated with sodium bicarbonate solution, which left undissolved a further quantity of the phenol (0·4 g.); the filtered solution was again acidified and extracted with ether Evaporation of the dried ethereal extract left an oil (1 g.), which formed a sparingly soluble *semicarbazone*. This crystallised from alcohol in well-formed prisms, decomp. 207—208° or, when rapidly heated, 215—216° (Found: C, 54·7; H, 8·1; N, 17·9. $C_{11}H_{19}O_3N_3$ requires C, 54·8; H, 7·9; N, 17·4%). Hydrolysis of the semicarbazone with sulphuric acid (10%) gave the *keto-acid*, which crystallised from dilute methyl alcohol in prismatic needles,

p. 105—107° (Found : C, 65·0; H, 8·6. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·7%). The acid identical with that prepared by the ozonolysis of hydroxyeremophilone benzoate (see below).

(c) *Ozonolysis of hydroxyeremophilone methyl ether.* The ether (7 g.) in methyl acetate (… c.c.) was ozonised at 0°. After decomposition of the ozonide the oil was dissolved in ether, and the ethereal extract washed successively with sodium carbonate and sodium hydroxide solutions. Evaporation of the dried extract gave hydroxyeremophilone methyl ether (2 g.). The sodium carbonate solution gave on acidification an acid (4·5 g.), from which the semicarbazone (0·6 g.) referred to above was prepared. The non-ketonic fraction of the acid was not further examined. From the sodium hydroxide solution, the phenol (0·5 g.) was isolated.

(d) *Ozonolysis of hydroxyeremophilone benzoate.* (i) The benzoate (2 g.) in carbon tetrachloride (20 c.c.) was ozonised at 0° until ozone was present in the issuing gases. After removal of the solvent from the deep yellow solution the ozonide in water (10 c.c.) was heated on the water-bath for 1 hour and then on the sand-bath for ½ hour. After cooling, the water was decanted from the resin, which, on shaking with ether, gave a crystalline solid (A) (0·7 g.). The ethereal extract was washed with sodium carbonate solution, which removed some benzoic acid, with sodium hydroxide solution (B), and the solvent removed, the residue (0·6 g.) being unchanged benzoate.

The solid (A), m. p. 175°, was recrystallised from alcohol (three times) and finally from ethyl acetate, from which it separated in long prismatic needles, m. p. 186—188° (Found : C, 69·5; H, 6·0. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·0%). The *oxide*, on hydrolysis with alcoholic potassium hydroxide solution, gave a small quantity of the keto-acid, $C_{10}H_{16}O_3$, characterised by the preparation of its semicarbazone, decomp. 207—208°.

The sodium hydroxide solution (B) gave, on acidification, a gum (0·3 g.) giving a deep red ferric chloride coloration. A semicarbazone was prepared which crystallised from methyl alcohol in prisms, m. p. 166° (Found : 61·3; H, 6·5%). This was not identified.

(ii) The benzoate (3 g.) in ethyl acetate (30 c.c.) was ozonised at 0° until an excess of ozone had passed through the solution for at least 4 hours. The yellow solution, which still contained a trace of undissolved benzoate, was filtered, and the solvent removed under diminished pressure. After decomposition with water on the water-bath the semicrystalline oil was dissolved in ether (oxalic acid was present in the aqueous solution) and the ethereal solution washed with sodium hydroxide solution. Evaporation of the solvent left a solid (0·1 g.) consisting of unchanged benzoate. The sodium hydroxide solution, after the addition of hydrogen peroxide (100-vol., 1 c.c.), was kept overnight, acidified, and extracted with ether; the dried ethereal extract on evaporation left an oil (2·8 g.). This was treated with an aqueous solution of semicarbazide acetate, a crystalline semicarbazone (1·7 g.) being rapidly deposited. This was collected and washed with ether, and the filtrate reserved. The semicarbazone crystallised from alcohol in prisms, decomp. 208—209°, and was identical with that prepared from the acid obtained by the oxidation of hydroxyeremophilone with chromic acid (see above). The *keto-acid*, obtained by hydrolysis of the semicarbazone with dilute sulphuric acid, crystallised from ligroin (b. p. 100—120°) or dilute methyl alcohol in needles, m. p. 105—107°, $[\alpha]_{5461}$ + 28·27° in methyl alcohol (*c*, 4·364) (Found : C, 65·2; H, 8·6. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·7%). The acid was sparingly soluble in cold water, somewhat readily in hot, and readily soluble in most of the ordinary organic solvents. It was stable to potassium permanganate in alkaline solution.

The solution from which the semicarbazone had been separated was repeatedly extracted with ether and this extract, combined with the ethereal washings from the semicarbazone, was, after removal of the solvent, distilled in steam. This removed benzoic acid; the cooled residue from the distillation was, after saturation with ammonium sulphate, extracted with ether. Removal of the solvent left a crystalline acid (0·2 g.). The *moloxide* of benzoic acid crystallised from water in needles, decomp. 230—232° after sintering at 200°. Two different specimens were analysed (Found : C, 54·2, 54·9; H, 3·7, 3·4. $C_7H_6O_4$ requires C, 54·5; H, 3·9%).

*Reduction of the Keto-acid.*—The keto-acid (1·7 g.), amalgamated zinc (20 g.), and hydrochloric acid (15 c.c.) were heated under reflux for 6 hours, a further quantity of acid (20 c.c.) then added, and the heating continued for 12 hours. From the cooled solution, ether extracted a liquid acid (1·4 g.) which was readily volatile in steam. To remove a little unchanged keto-acid, the oil was dissolved in ligroin (b. p. 40—60°), the solution filtered, and the ligroin removed. From the liquid acid, a p-*phenylphenacyl* ester was prepared which crystallised from

methyl alcohol in rosettes of leaflets, m. p. 65—67°, $[\alpha]_{5461}$ + 15·3° in ethyl acetate (*c*, 1·026) (Found : C, 78·9; H, 7·4. $C_{24}H_{28}O_3$ requires C, 79·1; H, 7·7%).

We are indebted to the Government Grants Committee of the Royal Society and to Imperial Chemical Industries Limited for grants.

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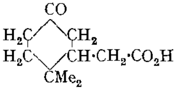
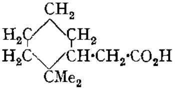
## 147. dl-2 : 2-*Dimethyl*cyclo*hexylacetic Acid.*

By P. S. ADAMSON, A. M. MARLOW, and J. L. SIMONSEN.

dl-2 : 2-*Dimethyl*cyclo*hexylacetic acid* has been synthesised and resolved into its optical enantiomorphs in order that the dextrorotatory form of the acid might be compared with an acid having the same composition obtained by the degradation of hydroxyeremophilone. The two acids were not identical.

BY the oxidation of the benzoate of hydroxyeremophilone Bradfield, Hellström, Penfold, and Simonsen (preceding paper) obtained a keto-acid, $C_{10}H_{16}O_3$, m. p. 105—107°, which they thought might be *d*-5-keto-2 : 2-dimethyl*cyclo*hexylacetic acid (I). Its product of reduction by the Clemmensen method was a liquid acid, $C_{10}H_{18}O_2$, which might be *d*-2 : 2-dimethyl*cyclo*hexylacetic acid (II). The *dl*-modification of the latter acid was readily prepared by

(I.)   (II.)

the condensation of 2 : 2-dimethyl*cyclo*hexanone (Cornubert, Bornel, and Bihan, *Bull. Soc. chim.*, 1931, **49**, 1385) with ethyl bromoacetate in the presence of zinc. The resulting *hydroxy*-ester, on dehydration with potassium hydrogen sulphate, yielded a mixture of ethyl 2 : 2-dimethyl*cyclo*hexylideneacetate and ethyl 2 : 2-dimethyl-$\Delta^6$-*cyclo*hexenylacetate, since oxidation gave 2 : 2-dimethyl*cyclo*hexanone, oxalic acid, and δ-acetyl-δ-methylhexoic acid, the last being identified by the preparation of its semicarbazone, decomp. 169° (Crossley and Renouf, J., 1911, **99**, 1111). Catalytic hydrogenation of the mixtnre of unsaturated esters gave *ethyl* dl-2 : 2-*dimethyl*cyclo*hexylacetate*, from which the dl-*acid* was obtained on hydrolysis. By means of the half molecule method the l-*ephedrine* salt of the lævorotatory form of the acid was easily obtained, and the pure d-*acid* was isolated in a similar manner *via* the *cinchonidine* salt. The p-*phenylphenacyl* esters of the *d*- and the *l*-acid had m. p. 87—88°, whereas the same derivative of the acid obtained from hydroxyeremophilone benzoate had m. p. 65—67°.

### EXPERIMENTAL.

For the preparation of 2 : 2-dimethyl*cyclo*hexanone the following modification of the method used by Cornubert *et al.* (*loc. cit.*) was adopted. To a mechanically stirred suspension of finely powdered sodamide (28 g.) in benzene (300 c.c.), 2-methyl*cyclo*hexanone (80 g.) was gradually added, the mixture being heated on the water-bath in a stream of dry nitrogen. After 3 hours evolution of ammonia ceased and methyl sulphate (100 g.) was slowly added to the cooled mixture (ice). After digestion for a further 3 hours ice was added to the neutral solution, and the benzene layer separated and shaken with concentrated aqueous ammonia to remove the excess of methyl sulphate. The benzene extract was washed with dilute sulphuric acid, sodium carbonate solution and water, and dried, and the solvent removed through a column. The residue (72 g.) had b. p. 162—169°/765 mm. The crude ketone was shaken mechanically with sodium bisulphite solution to remove unchanged 2-methyl*cyclo*hexanone (32 g.).

The methylated ketone (166 g.) which did not react with sodium bisulphite, was converted into the semicarbazone and this was fractionally crystallised from alcohol, yielding 2 : 2-dimethyl*cyclo*hexanonesemicarbazone (93 g.), m. p. 197—198°, which gave on hydrolysis with

sulphuric acid 2 : 2-dimethyl*cyclo*hexanone, b. p. 169—170°/768 mm., $d_{25^\circ}^{25^\circ}$ 0·9147, $n_D^{25^\circ}$ 1·4460. The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol in golden needles, m. p. 140—142° (Found : N, 18·0. $C_{14}H_{18}O_4N_4$ requires N, 18·3%).

*Ethyl* 1-*Hydroxy*-2 : 2-*dimethyl*cyclo*hexylacetate*.—Ethyl bromoacetate (35 g.) and 2 : 2-dimethyl*cyclo*hexanone (20 g.) were added to benzene (100 c.c.) containing zinc filings (12·5 g.) in suspension. On warming on the water-bath a vigorous reaction ensued, necessitating the removal of the source of heat; after this reaction had moderated, the mixture was heated for 4 hours, cooled, and mixed with an equal volume of dilute sulphuric acid (10%). The benzene layer was separated, washed with sodium bicarbonate solution and water, dried, and evaporated; the residue (25 g.) had b. p. 135—136°/18 mm. The *hydroxy*-ester was redistilled for analysis, b. p. 137°/20 mm. (Found : C, 67·0; H, 10·2. $C_{12}H_{22}O_3$ requires C, 67·3; H, 10·3%).

For the preparation of the unsaturated ester the hydroxy-ester (10 g.) was heated with finely powdered potassium hydrogen sulphate (10 g.) at 180—200° for 4 hours. After addition of water the oil was dissolved in ether, the ethereal solution washed with sodium carbonate solution, and dried, and the solvent evaporated. Analysis showed that the residual oil, b. p. 120—125°/18 mm., still contained some hydroxy-ester and it was therefore treated again with potassium hydrogen sulphate. The unsaturated *ester*, b. p. 121°/18 mm., was a mobile oil with a somewhat pungent odour (Found : C, 73·5; H, 10·0. $C_{12}H_{20}O_2$ requires C, 73·5; H, 10·2%).

*Ozonolysis of the Unsaturated Ester*.—The ester (2·3 g.) in methyl acetate was ozonised at 0° until excess of ozone passed freely through the solution. The solvent was removed under diminished pressure, and the ozonide mixed with water (5 c.c.) and decomposed by heating on the water-bath for 1 hour. Distillation in steam separated a volatile oil, identified as 2 : 2-dimethyl*cyclo*hexanone by the preparation of the semicarbazone and 2 : 4-dinitrophenylhydrazone. The residue from the steam distillation was a somewhat viscid oil giving a red coloration with ferric chloride. After digestion with dilute sulphuric acid (10%) for 1 hour to hydrolyse and decarboxylate the ester, the oil (0·6 g.) was isolated by ether in the usual manner and converted into the semicarbazone. δ-Acetyl-δ-methylhexoic acid semicarbazone crystallised from alcohol in rosettes of needles, decomp. 169° (Found : C, 52·7; H, 8·5. Calc. for $C_{10}H_9O_3N_3$ : C, 52·4; H, 8·3%).

dl-2 : 2-*Dimethyl*cyclo*hexylacetic Acid*.—The unsaturated ester (32·5 g.) in alcohol (120 c.c.) was shaken with hydrogen in the presence of palladium-norit (10%, 1 g.), the reduction being slow. After removal of the alcohol from the filtered solution, *ethyl* 2 : 2-*dimethyl*cyclo*hexylacetate* was obtained as a mobile oil, b. p. 122—123°/23 mm. (Found : C, 72·4; H, 11·0. $C_{12}H_{22}O_2$ requires C, 72·7; H, 11·1%). Hydrolysis of the ester with methyl-alcoholic potassium hydroxide solution in the usual manner gave dl-2 : 2-*dimethyl*cyclo*hexylacetic acid*, b. p. 153°/17 mm., which crystallised in needles, m. p. *ca*. 30° (Found : C, 70·6; H, 10·5. $C_{10}H_{18}O_2$ requires C, 70·6; H, 10·6%). The p-*phenylphenacyl* ester crystallised from methyl alcohol in needles, m. p. 86—87° (Found : C, 79·1; H, 7·7. $C_{24}H_{28}O_3$ requires C, 79·1; H, 7·7%). The *quinine* salt crystallised from ethyl acetate in needles, m. p. 97—100° after softening at 90°, $[\alpha]_{5461}$ − 125·3° in chloroform (*c*, 1·037) (Found : C, 69·1; H, 8·4. $C_{10}H_{18}O_2,C_{20}H_{24}O_2N_2,2H_2O$ requires C, 69·0; H, 8·8%).

l-2 : 2-*Dimethyl*cyclo*hexylacetic Acid*.—To a warm solution of the *dl*-acid (4·0221 g.) in water (30 c.c.) and alcohol (4 c.c.), sodium hydroxide solution (2·204N, 5·36 c.c.) and *l*-ephedrine (1·953 g.) were added. The *ephedrine* salt (3 g.), m. p. 87°, $[\alpha]_{5461}$ − 29·8° in alcohol (*c*, 3·291), crystallised on cooling; the mother-liquor deposited a further quantity (0·2 g.) of the salt on standing overnight. The salt (2·5 g.) crystallised from a mixture of benzene (17 c.c.) and ligroin (b. p. 60—80°, 100 c.c.) in fine needles (1·8 g.), m. p. 90—91°, $[\alpha]_{5461}$ −31·1° in alcohol (*c*, 3·277). This was unaltered by further crystallisation (Found : C, 67·9; H, 10·2. $C_{10}H_{18}O_2,C_{10}H_{15}ON,H_2O$ requires C, 68·0; H, 9·9%).

For the isolation of the acid, the salt (13 g.) was suspended in ether and shaken with an excess of 10% sodium hydroxide solution. The alkaline solution was separated and acidified with dilute sulphuric acid, and the liquid acid dissolved in ether. Evaporation of the ether from the dried extract gave l-2 : 2-*dimethyl*cyclo*hexylacetic acid* (5·6 g.), b. p. 149—150°/13 mm., m. p. *ca*. 43—44° after softening at 38°, $[\alpha]_{5461}$ − 14·57° in alcohol (*c*, 10·2). Attempts to recrystallise the acid failed (Found : C, 70·6; H, 10·5. $C_{10}H_{18}O_2$ requires C, 70·6; H, 10·6%). The p-*phenylphenacyl* ester crystallised from methyl alcohol in leaflets, m. p. 87—88°, $[\alpha]_{5461}$ −2·9° in ethyl acetate (*c*, 7·342) (Found : C, 79·0; H, 7·4. $C_{24}H_{28}O_3$ requires C, 79·1; H, 7·7%).

The acid recovered from the soluble ephedrine salt had b. p. 153°/18 mm., $[\alpha]_{5461}$ + 5·7° in alcohol (*c*, 3·610).

d-2 : 2-*Dimethyl*cyclo*hexylacetic Acid*.—To a warm solution of the crude *d*-acid (1·09 g.) in

alcohol (3 c.c.), sodium hydroxide solution (2·204N, 0·88 c.c.) and cinchonidine (1·31 g.) were added. The salt (1·2 g.) rapidly crystallised and a second fraction (0·8 g.) separated from the mother-liquor on long standing. The first fraction of the *cinchonidine* salt crystallised from ethyl acetate (5 c.c.) in rosettes of prismatic needles, m. p. 120—122°, $[\alpha]_{5461}$ −85·7° in alcohol (*c*, 1·241). A further crystallisation from ethyl acetate raised the rotatory power to 86·6° in alcohol (*c*, 1·254) and this together with the m. p. was unaltered by a further crystallisation (Found: C, 72·6; H, 8·8. $C_{10}H_{18}O_2,C_{19}H_{22}ON_2,H_2O$ requires C, 72·2; H, 8·7%). The second fraction of the salt, after crystallisation from ethyl acetate, had m. p. *ca.* 105°, $[\alpha]_{5461}$ −86·6°.

For the separation of the acid the cinchonidine salt was decomposed with sodium hydroxide solution, the cinchonidine extracted with chloroform, the alkaline solution acidified, and the d-*acid* dissolved in ether. After removal of the solvent the acid had b. p. 150°/13 mm., m. p. *ca.* 37—40°, $[\alpha]_{5461}$ + 14·1° in alcohol (*c*, 10·36) (Found: C, 70·7; H, 10·6. $C_{10}H_{18}O_2$ requires C, 70·6; H, 10·6%). The p-*phenylphenacyl* ester crystallised from methyl alcohol in leaflets m. p. 87—88° (Found: C, 79·0; H, 7·5. $C_{24}H_{28}O_3$ requires C, 79·1; H, 7·7%).

We are indebted to the Government Grants Committee of the Royal Society and to Imperial Chemical Industries Limited for grants and one of us (P. S. A.) thanks the Department of Scientific and Industrial Research for a maintenance allowance.

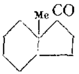
University College of North Wales, Bangor. [*Received, April 4th,* 1938.]

## 148. 2 : 2-*Dimethyl*cyclo*hexylacetic Acid.*

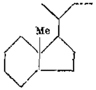
By G. H. Elliott and R. P. Linstead.

In connection with the synthesis of compounds containing a side chain similar to that present in the bile acids, 2 : 2-dimethyl*cyclo*hexanone has been treated with ethyl bromoacetate and magnesium, and 2 : 2-dimethyl*cyclo*hexylidene- and 2 : 2-dimethyl*cyclo*hexyl-acetic acids prepared. The former yields 2 : 2-dimethyl*cyclo*hexanone on oxidation, hence no molecular rearrangement occurs during the preparation. The latter acid is identical with that prepared by Adamson, Marlow, and Simonsen (preceding paper).

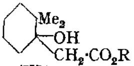
8-Methyl-1-hydrindanone (I) appeared a convenient starting point for the preparation of substances containing the carbon skeleton (II), which would serve as models for the synthesis of bile acids and similar compounds. Before employing this valuable ketone it seemed advisable to carry out parallel experiments on the more easily accessible 2 : 2-dimethyl*cyclo*hexanone, which also contains a quaternary carbon atom adjacent to a cyclic carbonyl group. What particularly interested us was whether it would be possible to dehydrate the hydroxy-ester (III, R = Et), obtained by the Reformatsky reaction, or the corresponding acid, without a retropinacolic change. The danger of this was indicated by Meerwein's well-known demonstration (*Annalen*, 1914, **405**, 142) that 2 : 2-dimethyl-*cyclo*hexanol gave, *inter alia*, 1 : 2-dimethyl*cyclo*hexene on dehydration. By analogy, the dehydration product of (III) might be a 1 : 2-dimethyl*cyclo*hexenyl-1-acetic acid derivative.



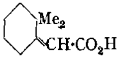

(I.)




(II.)




(III.)




(IV.)

To avoid this, the crystalline hydroxy-acid (III, R = H) was dehydrated with acetic anhydride, following Wallach (*Annalen*, 1909, **365**, 261). This yielded 2 : 2-*dimethyl*-cyclo*hexylideneacetic acid* (IV) as a crystalline solid, the structure of which was proved by its oxidation to 2 : 2-dimethyl*cyclo*hexanone.

At this stage in our work, Professor Simonsen informed us of his parallel experiments, described in the preceding paper. To unite the two pieces of work we reduced our αβ-unsaturated acid (IV). The 2 : 2-dimethyl*cyclo*hexylacetic acid so obtained melted rather higher than the material prepared by Adamson, Marlow, and Simonsen (preceding paper),

but the identity of the products was proved by comparison of the crystalline *p*-phenylphenacyl esters.

We also examined the reaction between 2 : 2-dimethyl*cyclo*hexanone and ethyl α-bromopropionate under Reformatsky conditions, but the yield was poor, and such reactions on ketones containing shielded carbonyl groups do not at the moment appear particularly promising for synthetic purposes.

EXPERIMENTAL.

Crude 2 : 2-dimethyl*cyclo*hexanone (Cornubert, Borrel, and Le Bihan, *Bull. Soc. chim.*, 1931, **49**, 1381) was purified through the 6-carboxylic ester as follows: A mixture of 200 g. of the crude ketone (b. p. 68—73°/21 mm.) with 250 g. of ethyl oxalate was treated at −10° during 2 hours with sodium ethoxide (34 g. of sodium and 520 c.c. of absolute alcohol). The product was kept for 2 days at 0° and for a day at room temperature, moisture being excluded, and then poured into a slight excess of dilute acid. The material extracted by ether was washed with water, dried (sodium sulphate), freed from solvent and low-boiling substances, and heated under reflux at 200° until no more carbon monoxide came off. Two fractionations of the product gave 103 g. of the 6-carboxylic ester, b. p. 125—128°/20 mm. This was hydrolysed and decarboxylated at the b. p. with an equal weight of baryta dissolved in 10 parts of water. 2 : 2-Dimethyl*cyclo*hexanone, isolated by means of ether, boiled at 67°/19 mm. (49 g.) and yielded a semicarbazone, m. p. 203° (Meerwein, *loc. cit.*, gives 201°).

18 G. of the pure ketone were warmed with ethyl bromoacetate (38 g.) and magnesium (5 g.) in 75 c.c. of dry benzene. After the vigour of the reaction had abated the mixture was refluxed for an hour, and the hydroxy-ester isolated in the usual manner. This was hydrolysed without purification with 80 c.c. of 20% aqueous potassium hydroxide in the cold for 24 hours and the crude acid, freed from neutral material, was esterified with 100 c.c. of 7% alcoholic sulphuric acid (6 hours at the b. p.). The *ethyl* 1-*hydroxy*-2 : 2-*dimethyl*cyclo*hexyl*-1-*acetate* (III, R = Et) (5·5 g.) was isolated by distillation, b. p. 136—140°/16 mm. (Found: C, 66·9; H, 10·3. $C_{12}H_{22}O_3$ requires C, 67·3; H, 10·4%). This procedure separates the hydroxy-ester from auto-condensation products of the ketone. Hydrolysis of the pure ester with cold alcoholic potash yielded the corresponding *acid* (III, R = H), which immediately solidified; it formed rhombs from benzene–petrol, m. p. 99—100° (Found: C, 64·7; H, 9·9. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·7%).

The hydroxy-acid (3·2 g.) was refluxed for 3 hours with 8 c.c. of acetic anhydride. The unsaturated acid, isolated from the product by distillation in steam and extraction with ether, rapidly solidified. Yield, 2·0 g. 2 : 2-*Dimethyl*cyclo*hexylideneacetic acid* (IV) formed needles, m. p. 91—92°, from dilute acetic acid (Found: C, 71·3; H, 9·7. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6%). In keeping with the αβ-position of the double bond, a solution of the acid in aqueous sodium bicarbonate did not decolourise one of iodine in potassium iodide.

The unsaturated acid (1 g.), dissolved in a little water containing sodium bicarbonate (0·8 g.), was treated slowly with 55 c.c. of 3% aqueous potassium permanganate. After an hour the product was distilled in steam. The ketone was isolated by means of ether and identified as 2 : 2-dimethyl*cyclo*hexanone by conversion into the semicarbazone, m. p. and mixed m. p. 202—203°.

The acid (250 mg.) was reduced over Adams's catalyst in acetic acid, the theoretical quantity of hydrogen being absorbed within 24 hours. The solvent was removed at 60°, and the product, isolated by means of ether, crystallised immediately. 2 : 2-Dimethyl*cyclo*hexylacetic acid formed fern-shaped aggregates of needles, m. p. 45° (crude), 47° after crystallisation from dilute acetic acid. The *p*-phenylphenacyl ester, after crystallisation from ethyl alcohol, melted at 86—87°, alone or in admixture with a specimen kindly supplied by Professor Simonsen.

Condensation of 2 : 2-dimethyl*cyclo*hexanone with ethyl α-bromopropionate and magnesium under various conditions gave poor yields of hydroxy-ester. In one series of experiments 18 g. of the ketone yielded 5 g. of crude hydroxy-ester after hydrolysis and re-esterification by the method described above. This boiled at 100—140°/18 mm. and on hydrolysis yielded a gummy acid, which on dehydration with acetic anhydride gave 2 g. of an acid volatile in steam, which failed to solidify (Found: equiv., 187. $C_{11}H_{18}O_2$ requires equiv., 182·1).

We are indebted to Professor J. L. Simonsen, F.R.S., for the opportunity of comparing the products made by the two routes.

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# NOTES

## 1-*Methyl*-2-n-*propylphenanthrene*. By G. A. R. Kon, E. S. Narracott, and C. Reid.

1-*Methyl*-2-n-*propylphenanthrene*, which was required for comparison with a hydrocarbon isolated in the course of another research, has been prepared by a standard method. Ethyl *n*-propylmalonate was condensed with β-1-naphthylethyl bromide, the product hydrolysed and decarboxylated to γ-1-*naphthyl*-α-n-*propylbutyric acid*, the chloride of which was cyclised to 1-*keto*-2-n-*propyl*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*; this with methylmagnesium iodide gave a carbinol, which nnderwent dehydration to the *dihydro*-derivative of the required hydrocarbon; the final dehydrogenation was carried out with palladised charcoal.

100 G. of ethyl *n*-propylmalonate were added to 18·5 g. of "molecular" potassium in 250 c.c. of benzene; the mixtnre was warmed for ½ hour, then boiled for 48 hours with 75 g. of β-1-naphthylethyl bromide. The prodnct was isolated by addition of water and distillation of the benzene solntion. The fraction (33 g.), b. p. 203—211°/2·5 mm., was boiled with 25 g. of potassium hydroxide in 30 c.c. of water and enough alcohol to effect solution; 22 g. of β-1-*naphthylethyl*-n-*propylmalonic acid* were ultimately obtained as an oil, which soon solidified and had m. p. 173° (decomp.) after crystallisation from benzene–petroleum (Found : C, 71·9; H, 6·5. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7%).

Attempts to decarboxylate the acid by boiling with water (compare Fieser and Seligman, *J. Amer. Chem. Soc.*, 1935, **57**, 2174) failed and 35 g. of it were therefore heated above its m. p., and the product distilled under 2 mm. pressure, the yield of γ-1-*naphthyl*-α-n-*propylbutyric acid* being 25 g. This gradually solidified and crystallised from dilute alcohol in small rhombs, m. p. 68—69° (Found : C, 79·4; H, 8·0. $C_{17}H_{20}O_2$ requires C, 79·6; H, 7·9%).

25 G. of the preceding acid were left overnight with 10 c.c. of thionyl chloride in 200 c.c. of petroleum, the solution warmed for 1½ hours, and the solvent distilled under reduced pressure. The residue was taken up in 200 c.c. of carbon disulphide and treated with 10 g. of finely powdered aluminium chloride in small portions. After 12 hours, dilute hydrochloric acid was added, and 1-*keto*-2-n-*propyl*-1 : 2 : 3 : 4-*tetrahydrophenanthrene* isolated in the usual way (19 g.), b. p. 206—208°/5 mm.; it solidified at once and separated from dilute alcohol (charcoal) in lustrous plates, m. p. 53° (Found : C, 85·7; H, 7·8. $C_{17}H_{18}O$ requires C, 85·7; H, 7·6%); it formed a semicarbazone, m. p. 210—202°.

19 G. of the ketone in 100 c.c. of ether were dropped into a solution of the Grignard reagent prepared from 5·8 c.c. of methyl iodide, and the mixture then boiled for an hour. The prodnct was isolated in the usual way, treated with semicarbazide acetate to remove any unchanged ketone (none was found), and distilled under reduced pressure, some water then being eliminated. 1-*Methyl*-2-n-*propyl*-3 : 4-*dihydrophenanthrene* was finally distilled over sodium, b. p. 208—210°/13 mm.; in another preparation it was purified by percolation of a petroleum solution through a column of activated alumina, but it did not solidify (Found : C, 92·0; H, 8·2. $C_{18}H_{20}$ requires C, 91·5; H, 8·5%).

8 G. of the dihydro-compound were heated under reflux with 4 g. of 10% palladised charcoal for 4 hours at 250—300°. The product was then thoroughly extracted with petroleum (b. p. 40—60°), and the solution allowed to percolate through a 30 cm. column of activated alumina. On evaporation, 6 g. of 1-*methyl*-2-n-*propylphenanthrene* were recovered, which formed plates, m. p. 54°, from methyl alcohol (Found : C, 92·2, 92·3; H, 7·6, 7·5. $C_{18}H_{18}$ requires C, 92·3; H, 7·7%). The orange *picrate* had m. p. 97° (Found : C, 62·1; H, 4·4. $C_{18}H_{18},C_6H_3O_7N_3$ requires C, 62·2; H, 4·6%); the yellow *s*-trinitrobenzene *complex* formed needles, m. p. 112°, from methyl alcohol (Found : C, 64·9; H, 4·7. $C_{18}H_{18},C_6H_3O_6N_3$ requires C, 64·4; H, 4·7%), the trinitrotoluene *complex*, pale yellow needles, m. p. 82—83°, from methyl alcohol (Found : C, 65·3; H, 5·0. $C_{18}H_{18},C_7H_5O_6N_3$ requires C, 65·0; H, 5·0%), and the *styphnate*, dark yellow needles, m. p. 118—119°, from methyl alcohol (Found : C, 60·1; H, 4·2. $C_{18}H_{18},C_6H_3O_8N_3$ requires C, 60·1; H, 4·4%).

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*An Improved Method for the Preparation of α-Chlorocrotonic Acid.* By JOHN C. ROBERTS.

HE method for the preparation of α-chlorocrotonic acid given in Beilstein's "Organische hemie," involving reaction between butylchloral hydrate and potassium ferrocyanide (Wallach, *Ber.*, 1877, **10**, 1530), is troublesome and gives poor yields when fairly large quantities of the cid are required. The following method (compare Krämer and Pinner, *Annalen*, 1871, **158**, i0) gives superior results.

Butylchloral hydrate (50 g.), when added to 100 c.c. of nitric acid (*d*, 1·504), dissolves easily and the solution becomes cold. This is kept at 30—35° for 1½ hours with intermittent shaking and at the ordinary temperature for 24 hours; the acid is then distilled until the temperature of the vapour is 135°. The residue, on cooling, forms colourless crystals of trichlorobutyric acid (47 g.). This is mixed with 200 c.c. of water (it does not dissolve completely and a lower oily layer forms), and zinc dust (30 g.) slowly added; a vigorous reaction occurs. The mixture is heated on a water-bath for 3 hours and cooled, concentrated hydrochloric acid (30 c.c.) added, and the α-chlorocrotonic acid extracted with ether (70 + 50 + 40 c.c.). The combined extracts are washed with water and dried (sodium sulphate), the solvent evaporated, and the product dried over concentrated sulphuric acid in a desiccator. The α-chlorocrotonic acid (26 g.) has m. p. 99—100° (Wislicenus, *Annalen*, 1888, **248**, 293, gives 99·2°). Yield, 83·5% of the theoretical, calculated on the butylchloral hydrate. The ethyl ester has b. p. 174—176° (corr.) [Perkin, J., 1894, **65**, 424, gives 175—176° (corr.)].

The method is superior to that of Wallach in that (i) the evolution of large quantities of hydrogen cyanide is avoided and (ii) the yield of α-chlorocrotonic acid is nearly doubled (Wallach's method gives 44·3% of the theoretical yield).—UNIVERSITY COLLEGE, NOTTINGHAM.

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# 149. *The Kinetics of Two Ionic Exchange Reactions of the Methyl Halides in Water.*

By E. A. MOELWYN-HUGHES.

The replacement of bromine in methyl bromide by the iodide ion in aqueous solution is a bimolecular reaction which is opposed by the interaction of methyl iodide and the bromide ion, and complicated by the simultaneous hydrolysis of both methyl halides. The velocity constants for the two bimolecular reactions have been determined over a range of temperatures, and yield energies of activation, which, although possibly in error by a few hundred calories, are of sufficient accuracy for the purpose of comparison with similar figures for the reactions of the same halides with other ions.

THE kinetics of the reactions of the methyl halides with other molecules, atoms, or ions, which we are now systematically investigating, are somewhat less complicated than those of the other *n*-alkyl halides, owing to the impossibility of olefin formation. In hydroxylic media, however, even the methyl halides react with solvent molecules, and quantitative allowance for this simultaneous reaction must be made in any careful study of such systems. The present paper describes the results of experiments on the replacement of the halogen atom in methyl bromide and methyl iodide by another halogen atom. Concurrent with the opposing bimolecular changes are the two unimolecular hydrolytic reactions, so that the kinetic scheme is as follows:

$$\begin{array}{ccc} CH_3Br + I^- & \underset{k_4}{\overset{k_2}{\rightleftharpoons}} & CH_3I + Br^- \\ \downarrow k_1 & & \downarrow k_3 \\ CH_3{\cdot}OH + H^+ + Br^- & & CH_3{\cdot}OH + H^+ + I^- \end{array}$$

The magnitudes of the hydrolysis constants, $k_1$ and $k_3$, are known (Moelwyn-Hughes, *Proc. Roy. Soc.*, 1938, *A*, **164**, 295); and by means of chemical analysis and the velocity equations

$$+\,d[I^-]/dt = k_3[CH_3I] + k_4[CH_3I][Br^-] - k_2[CH_3Br][I^-] \quad . \quad . \quad (1)$$

$$+\,d[Br^-]/dt = k_1[CH_3Br] + k_2[CH_3Br][I^-] - k_4[CH_3I][Br^-] \quad . \quad . \quad (2)$$

the constants $k_2$ and $k_4$ have been evaluated over the workable ranges of temperature and concentration.

## Experimental.

Solutions of the methyl halides in water were prepared in the apparatus previously described. By means of the distribution coefficients given in the previous paper, it was possible, by adjustment of the vapour pressure, to prepare solutions of the desired concentration. In order to avoid a measurable extent of hydrolysis during dissolution, the solutions were sometimes removed before they had reached the saturation point. Solutions of potassium bromide and iodide were made by weight. The two reactants were mixed after short storage in ice, and sealed off in glass tubes of about 20 c.c. capacity. Check experiments are required to obtain accurate zero-time corrections—a factor of some importance for bimolecular mechanisms. After immersion for a measured time in the thermostat, the tubes were cooled in ice, and the contents analysed for total halide by Volhard's method, for inorganic iodide by the iodate method, and for hydrogen ion. The standard solutions were about N/100. Attention to the details of the volumetric analyses (for which I am much indebted to Mr. A. J. Berry) enables the concentrations of solutes to be estimated to a fraction of a millimole per litre. This is the unit of concentration used in this work.

The simple kinetic scheme outlined above must satisfy two requirements: (1) The final concentration of that inorganic ion which is present at the start must equal its initial concentration: this condition is demanded by the effective irreversibility of the hydrolyses. (2) Over the whole range of reaction the following equation must hold:

$$[Br^- + I^-]_t - [I^-]_0 = [H^+]_t \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The initial and final concentrations of inorganic halides for a few experiments are shown in Table I, from which it is seen that equation (3) is more closely followed when bromide ion is present initially than when iodide ion is present initially. The figures in cols. 3 and 6 show that the apparent concentration of bromide ions and the actual concentration of iodide ions are, respectively, greater and less at the end of the reaction than at the beginning. Both

Table I.

| $[Br^-]_0$. | $[Br^-]$. | Diff. | $[I^-]_0$. | $[I^-]$. | Diff. |
|---|---|---|---|---|---|
| 26·3 | 26·3 | 0 | 49·6 | 47·5 | −2·1 |
| 50·6 | 50·8 | +0·2 | 50·0 | 49·1 | −0·9 |
| 52·1 | 52·4 | +0·3 | 50·2 | 48·2 | −2·0 |
| 99·6 | 100·2 | +0·6 | 50·5 | 49·7 | −0·8 |
| 99·8 | 100·3 | +0·5 | 50·8 | 49·1 | −1·7 |
| 99·9 | 100·7 | +0·8 | 99·5 | 99·2 | −0·3 |
| 103·0 | 104·2 | +1·2 | 151·0 | 144·6 | −6·4 |

discrepancies have a common origin in the oxidation of the iodide ion, chiefly, if not entirely, to molecular iodine. Titration with thiosulphate after chloroform extraction, gave, *e.g.*, the values 2·0 and 5·7 for $[I_2]$, corresponding to the first and the last entry in col. 6. The present technique for working with the solutions of volatile vapours does not allow of the complete elimination of atmospheric oxygen. The effect of this side reaction on the course and velocity of the ionic exchange reaction is, however, slight, for, as seen in Table II, the oxidation reaction is relatively slow, and plays no appreciable part during such times as are required for substitution.

Table II.

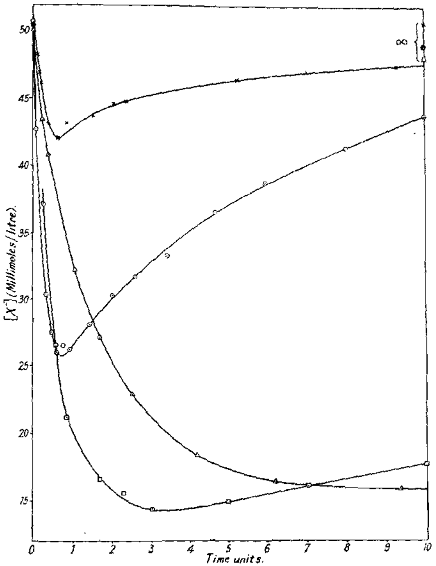
$T = 323·37°$ K. $[I^-]_0 = 50·5$. $[CH_3Br]_0 = 52·7$.

| *t*, mins. | $[I^-]$. | $[I^- + Br^-]$. | $[H^+]$. | $[I^- + Br^-] - [I^-]_0$. |
|---|---|---|---|---|
| 0 | 50·4 | 50·6 | 0·2 | 0·1 |
| 7 | 43·8 | 50·9 | 0·5 | 0·4 |
| 10 | 40·3 | 51·7 | 0·6 | 1·2 |
| 13 | 38·3 | 51·1 | 0·4 | 0·6 |
| 23 | 33·4 | 51·0 | 0·6 | 0·5 |
| 33 | 28·3 | 51·3 | 1·4 | 0·8 |
| 43 | — | 51·8 | 1·4 | 1·3 |
| 63 | 19·3 | 52·3 | 1·8 | 1·8 |
| 83 | 14·7 | 52·6 | 2·3 | 2·1 |
| 153 | 13·9 | 53·8 | 3·1 | 3·3 |
| 233 | 12·8 | 55·5 | 4·5 | 5·0 |
| 393 | 12·2 | 56·8 | 5·8 | 6·3 |
| 1333 | 19·0 | 65·5 | 17·6 | 15·0 |
| ∞ | 49·7 | 103·2 | 49·0 | 52·7 |

$T = 362·46°$ K. $[I^-]_0 = 50·8$. $[CH_3Br]_0 = 35·6$.

| *t*, mins. | $[I^-]$. | $[I^- + Br^-]$. | $[H^+]$. | $[I^- + Br^-] - [I^-]_0$. |
|---|---|---|---|---|
| 0 | 50·8 | 50·8 | 0 | 0 |
| 1 | 42·8 | 52·8 | 2·2 | 2·0 |
| 4 | 30·4 | 53·5 | 3·6 | 2·7 |
| 5·5 | 27·6 | 54·8 | 3·8 | 4·0 |
| 7 | 26·0 | 55·4 | 4·6 | 4·6 |
| 9 | 26·6 | 56·4 | 5·5 | 5·6 |
| 11 | 26·3 | 57·9 | 5·8 | 7·1 |
| 17 | 28·2 | 59·4 | 8·4 | 8·6 |
| 24 | 30·3 | 61·4 | 10·6 | 10·6 |
| 31 | 31·7 | 63·3 | 12·5 | 12·5 |
| 41 | 33·3 | 66·4 | 15·1 | 15·6 |
| 56 | 36·6 | 68·8 | 18·4 | 18·0 |
| 71 | 38·8 | 72·4 | 21·0 | 21·6 |
| 96 | 41·4 | 75·8 | 25·1 | 25·0 |
| 121 | 44·1 | 78·4 | 26·1 | 27·6 |
| ∞ | 49·1 | 86·4 | — | 35·6 |

The results of a few typical experiments are shown graphically in the figure, where the icentration of that halide ion which was present initially is shown as a function of the time. e plots of the concentrations of organic halide against time, would, of course, be nearly the rror images of these curves. From the analytical data it is possible, but unnecessary, to




× T = 324·52° K. *Time unit* = 300 *mins.* $[CH_3I]_0$ = 39·6. $[Br^-]_0$ = 50·7.
⊙ T = 362·46° K. *Time unit* = 12 ,, $[CH_3Br]_0$ = 35·6. $[I^-]_0$ = 50·8.
⊡ T = 340·01° K. *Time unit* = 12 ,, $[CH_3Br]_0$ = 48·4. $[I^-]_0$ = 50·0.
△ T = 308·61° K. *Time unit* = 120 ,, $[CH_3Br]_0$ = 41·1. $[I^-]_0$ = 50·2.

reproduce for any given experiment graphs showing the variation in the concentrations of all six solutes with time. The course of the curve formed by the time-variation of the concentration of the liberated ion, is, however, of interest; it rises rapidly to a stationary value, after which it rises with the slower velocity that is quantitatively in agreement with that of the hydrolysis of the organic halide.

TABLE III.

| *T* = 308·61° K. | | | | *T* = 298·03° K. | | | |
|---|---|---|---|---|---|---|---|
| *t*, mins. | $[I^-]$. | $[I^- + Br^-]$. | $[Br^-]$. | *t*, mins. | $[I^-]$. | $[I^- + Br^-]$. | $[Br^-]$. |
| 0 | 0 | 99·6 | 99·6 | 0 | 0 | 99·6 | 99·6 |
| 25 | 1·3 | | 98·3 | 30 | 0·8 | 99·7 | 98·9 |
| 35 | 2·0 | | 97·6 | 67 | 1·2 | 99·9 | 98·7 |
| 105 | 4·7 | | 94·9 | 233 | 2·4 | 99·8 | 97·4 |
| 165 | 6·8 | 99·6 | 92·8 | 1165 | 8·3 | 100·0 | 91·7 |
| 415 | 11·8 | 100·2 | 88·4 | 1680 | 10·0 | 100·5 | 90·5 |
| 852 | 14·0 | 101·0 | 87·0 | 4020 | 12·9 | 101·3 | 88·4 |
| 1313 | 15·1 | 102·0 | 86·9 | ∞ | 55·1 | 155·4 | 100·3 |
| ∞ | 58·4 | 158·6 | 100·2 | | | | |

With solutions containing initially no iodide ion, the oxidation process is entirely negligible at low temperatures, and direct estimation of hydrogen ion for each sample is unnecessary. Some typical figures are shown in Table III, from which it is clear that under these conditions the exchange reaction passes its half-life without interference by the hydrolysis.

*Determination of the Ratio*, $k_2/k_4$.—In a study of opposing reactions, the determination of the ratio of the two velocity constants conveniently precedes the absolute evaluation of either. Numerous methods are available; the first one to be employed is as follows.

Two complementary experiments were carried out at 308·61° K., the reaction being allowed to start from opposite ends. In both cases the concentration of the inorganic halide decreased to a stationary value. With $[I^-]_0 = 50·2$ and $[CH_3Br]_0 = 40·1$, the stationary-state concentrations are reached after 1150 minutes, and yield the ratio

$$\{[Br^-][CH_3I]/[I^-][CH_3Br]\}_{I^-} = 36·1 \times 34·7/15·5 \times 4·1 = 19·7$$

For the other experiment, with $[Br^-]_0 = 99·6$ and $[CH_3I]_0 = 58·4$, the values are

$$\{[Br^-][CH_3I]/[I^-][CH_3Br]\}_{Br^-} = 87·0 \times 43·8/14·9 \times 12·6 = 20·3$$

To conclude from these figures that $k_2/k_4 = 20·0 \pm 0·3$ is, however, fallacious, for the figures show the incidence of hydrolysis to the extents 1·4 and 2·3 millimoles per litre respectively. The inequality of the two ratios is genuine, and, provided it can be magnified, may be used to determine the ratio of the bimolecular constants.

Let the ratio of the concentrations (as written above) which correspond to the minimal concentration of iodide ion be denoted by $R_{I^-}$, and the same ratio corresponding to the minimal concentration of bromide ion by $R_{Br^-}$; then, by equations (1) and (2) we have

$$k_2/k_4 = R_{I^-}\{1 + k_3/k_4[Br^-]_{I^-}\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

and

$$k_2/k_4 = R_{Br^-} - k_1/k_4[I^-]_{Br^-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

For a pair of experiments at 340·01° K., it was found that $[I^-]_0 = 50·0$; $[CH_3Br]_0 = 48·4$; $R_{I^-} = 10·9$; $[Br^-]_0 = 99·9$; $[CH_3I]_0 = 52·5$; $R_{Br^-} = 14·6$. Full allowance being made for the experimental error, these figures suffice to fix the ratio $k_2/k_4$ as 13·3 ± 0·3 at this temperature. At lower temperatures, fairly reliable values of the ratio may be found from experiments on the initial rates with halide ions in excess. The best values found by both methods are summarised in Table IV, along with those given by the empirical relation

$$k_2/k_4 = 2·79 \times e^{-1,050/RT} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

TABLE IV.

| | | | | | | |
|---|---|---|---|---|---|---|
| $T$ | | 293·53° | 298·19° | 308·61° | 323·95° | 340·01° |
| $k_2/k_4$ | Obs. | 16·9 | 16·5 | 15·4 | 14·3 | 13·3 |
| | By formula | 16·9 | 16·4 | 15·5 | 14·3 | 13·2 |

The energy term in the formula is to be regarded as the minimum value, and may be as much as 630 cals. low. Uncertainties in the energy amounting to this are unavoidable when the ratio of the constants differs widely from unity, as is seen from the figures in Table V, where stationary concentrations (denoted by subscript S) found experimentally at some of the lower temperatures are compared with the values (shown in parentheses) calculated from the approximate relation

$$[Br^-]_S[CH_3I]_S/[I^-]_S[CH_3Br]_S \approx k_2/k_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

In the majority of cases, the stationary concentration of the alkyl halide is less than that calculated from the approximate formula (7), as is to be expected.

*Determination of the Constants* $k_2$.—The two methods found most suitable for the evaluation of the bimolecular constant, $k_2$, are: (i) The determination of the position of minima for solutions with different initial concentrations at the same temperature; equations (4) and (5) are directly applicable, irrespective of the extent of hydrolysis, and yield reliable absolute values of the constants at the higher temperatures. (ii) The determination of the bimolecular constant for a system of opposing reactions, only those

TABLE V.

| $T$. | $[Br^-]_0$. | $[CH_3I]_0$. | $[I^-]_0$. | $[CH_3Br]_0$. | $[Br^-]_e$. | $[CH_3I]_e$. | $[I^-]_e$. | $[CH_3Br]_e$. |
|---|---|---|---|---|---|---|---|---|
| 293·21° | 0 | 0 | 150·7 | 59·6 | 57·3 (57·5) | 57·2 (57·5) | 93·5 (93·2) | 2·3 (2·1) |
| | 2·0 | 0 | 49·5 | 47·2 | 41·2 (40·6) | 37·2 (38·6) | 12·3 (10·9) | 8·0 (8·6) |
| | 26·3 | 27·3 | 0 | 0 | 21·9 (21·1) | 22·9 (22·1) | 4·4 (5·2) | 4·4 (5·2) |
| | 52·1 | 52·1 | 0 | 0 | 41·2 (41·9) | 40·5 (41·9) | 11·6 (10·2) | 10·9 (10·2) |
| | 100·3 | 51·7 | 0 | 0 | 89·1 (88·9) | 37·8 (37·7) | 13·9 (14·1) | 13·9 (14·1) |
| 298·11 | 0 | 0 | 100·8 | 50·4 | 47·7 (47·8) | 46·7 (47·8) | 54·1 (53·1) | 2·7 (2·7) |
| | 99·7 | 56·0 | 0 | 0 | 88·2 (85·0) | 42·4 (41·3) | 13·6 (14·7) | 11·5 (14·7) |
| 308·61 | 0 | 0 | 50·2 | 40·1 | 36·1 (35·5) | 34·7 (35·5) | 15·5 (14·7) | 4·0 (4·6) |
| | 99·6 | 58·7 | 0 | 0 | 87·0 (84·2) | 43·8 (43·3) | 14·9 (15·4) | 12·6 (15·4) |

values being accepted which refer to stages where hydrolysis can legitimately be ignored. Denoting by $a$ and $b$ the initial concentrations of methyl bromide and iodide ion respectively, and by $x$ the amount of bromide ion at time, $t$, we have

$$\underset{(a-x)}{CH_3Br} + \underset{(b-x)}{I^-} \underset{k_4}{\overset{k_2}{\rightleftharpoons}} \underset{x}{CH_3I} + \underset{x}{Br^-}$$

$$+\,\mathrm{d}x/\mathrm{d}t = k_2(a-x)(b-x) - k_4x^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

which gives on integration

$$x = ab/\{A + B\coth[tB(k_2 - k_4)]\}(1 - K) \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

where $K = k_4/k_2$, $A = (a + b)/2(1 - K)$, and $B = \{(a - b)^2 + 4Kab\}^{\frac{1}{2}}/2(1 - K)$.

Two examples of the applicability of this equation for the early stages of experiment are illustrated in Table VI, from which average values of $3{\cdot}71 \times 10^{-4}$ and $7{\cdot}02 \times 10^{-4}$ have been obtained for $k_2$, expressed in l./mole-sec.

TABLE VI.

$T = 292{\cdot}3°$ K. $a = 47{\cdot}2$. $b = 49{\cdot}6$. $k_2/k_4 = 17{\cdot}0$.

| $t$ (mins.). | $x$. | $10^4k_2$ (l./mole-sec.). |
|---|---|---|
| 0 | 0 | — |
| 40 | 1·9 | 3·62 |
| 80 | 3·8 | 3·73 |
| 115 | 5·4 | 3·78 |
| 140 | 6·3 | 3·70 |
| 370 | 14·3 | 3·92 |
| 460 | 15·7 | 3·53 |
| 1580 | 27·2 | 2·91 |
| 2880 | 31·0 | 2·30 |
| 4380 | 35·2 | 2·51 |

$T = 298{\cdot}19°$ K. $a = 50{\cdot}4$. $b = 100{\cdot}8$. $k_2/k_4 = 16{\cdot}4$.

| $t$ (mins.). | $x$. | $10^4k_2$ (l./mole-sec.). |
|---|---|---|
| 0 | 0 | — |
| 20 | 4·1 | 7·18 |
| 38 | 7·2 | 6·95 |
| 136 | 20·5 | 7·04 |
| 306 | 32·5 | 7·11 |
| 435 | 37·0 | 6·81 |
| 845 | 43·8 | 6·40 |

The data in Table VII show the extent to which the constants $k_2$ may be reproduced by the equation

$$k_2 = 1{\cdot}68 \times 10^{10} \times e^{-18{,}260/RT} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

TABLE VII.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| $T$ .......................... | 273·6° | 292·30° | 293·53° | 298·19° | 308·61° | 323·37° | 340·01° |
| $k_4 \times 10^4$ Obs. ........... | 0·453 | 3·71 | 4·26 | 7·02 | 20·0 | 77·6 | 312 |
| $k_4 \times 10^4$ By formula ... | 0·442 | 3·68 | 4·31 | 7·00 | 20·2 | 76·8 | 313 |

The apparent energy of activation, $E_2$, is accurate to within $\pm$ 130 cals., and $(\delta E_2/\delta T)_I$ must lie within the rather wide limits $\pm$ 6·9 cals./mole-degree.

*Determination of the Constants* $k_4$.—Measurements of the constants $k_4$ present greater difficulties because (i) the extent of chemical change is less, and (ii) on account of the low value of $k_4$, the hydrolytic complication is relatively greater. For the simple kinetic system

$$\underset{(c-y)}{CH_3I} + \underset{(d-y)}{Br^-} \underset{k_2}{\overset{k_4}{\rightleftarrows}} \underset{y}{CH_3Br} + \underset{y}{I^-}$$

we have
$$+ dy/dt = k_4(c-y)(d-y) - k_2y^2$$

which gives on integration

$$y = cd/\{C + D \coth [tD(k_2 - k_4)]\}(L-1) \quad . \quad . \quad . \quad . \quad . \quad (11)$$

where $L = k_2/k_4$, $C = (c+d)/2(L-1)$, and $D = \{(c-d)^2 + 4Lcd\}^{\frac{1}{2}}/2(L-1)$.

The use of this formula, with the values of $L$ given by equation (6), leads to initial values of $k_4$ which, though falling with time as required, show no regular decline from which a reliable initial figure can be obtained. With the experimental ratio of the stationary concentrations, however, the method gives moderately good results. Examples of both types of figures are shown in Table VIII, where interpolated values of $y$ are used. In view of the inherent difficulties, the final values of $k_4$ (Table IX) are in satisfactory agreement with those anticipated by combining equations (6) and (10), *viz.*,

$$k_4 = 6{\cdot}02 \times 10^9 \times e^{-19{,}310/RT} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

The apparent energy of activation, $E_4$, lies near the lower of the two limits, which are 19,170 and 20,060 cals./mole. The uncertainty in the true value of the energy of activation is thus of the same order of magnitude as the correction which appears necessary for the electrostatic contribution, which amounts to $N_0 z_B \varepsilon \mu_A \cos \theta (LT-1)(1-\frac{1}{2}\kappa r)e^{-\kappa r}/D$ (Moelwyn-Hughes, *Proc. Roy. Soc.*, 1936, *A*, **157**, 667).

TABLE VIII.

| $T = 298{\cdot}03°$ K. $c = 56{\cdot}0$. $d = 99{\cdot}7$. $k_2/k_4 = 16{\cdot}4$. | | | $T = 308{\cdot}61°$ K. $c = 58{\cdot}7$. $d = 99{\cdot}6$. $k_2/k_4 = 20{\cdot}0$. | | |
|---|---|---|---|---|---|
| $t$ (mins.). | $y$. | $10^5k_4$ (l./mole-sec.). | $t$ (mins.). | $y$. | $10^4k_4$ (l./mole-sec.) |
| 0 | 0 | — | 0 | 0 | — |
| 260 | 2·7 | 3·25 | 76 | 3·6 | 1·44 |
| 560 | 4·7 | 2·75 | 130 | 5·6 | 1·39 |
| 960 | 6·7 | 2·44 | 199 | 7·6 | 1·33 |
| 1560 | 8·7 | 2·12 | 280 | 9·6 | 1·34 |
| 2800 | 10·7 | 1·64 | 404 | 11·6 | 1·35 |

TABLE IX.

| | | | | |
|---|---|---|---|---|
| $T$ | 293·53° | 308·61° | 324·52° | 340·01° |
| $k_4 \times 10^4$ Obs. | 0·269 | 1·35 | 6·70 | 24·1 |
| $k_4 \times 10^4$ By formula | 0·257 | 1·29 | 6·02 | 23·4 |

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## 150. *Liquid-phase Reactions at High Pressures. Part III. The Esterification of Acetic Acid.*

By SHU-LIN P'ENG, R. H. SAPIRO, R. P. LINSTEAD, and D. M. NEWITT.

The rate of esterification of acetic acid with a series of primary and secondary aliphatic alcohols has been measured at pressures from 1 to 4000 atmospheres, and at temperatures between 70° and 80°. The velocity constants for the *n*-primary alcohols are all of the same order, tending, if anything, to diminish as the series is ascended; *iso*propyl and *sec.*-butyl alcohols have much lower constants than the primary alcohols.

The accelerating effect of pressure becomes less marked on ascending the series of primary alcohols; it is greater for *iso*- and *sec.*-alcohols than for primary alcohols.

For all the reactions studied, the constants $A$ and $E$ of the Arrhenius equation ($k = Ae^{-E/RT}$) increase with pressure, the effect being greatest with *iso*propyl and *sec.*-butyl alcohols. The cause of this increase is discussed, and it is shown that although the increase in $A$ can, in some instances, be accounted for by an increase in the collision frequency with pressure, yet in other cases the probability that collisions between molecules possessing the requisite amount of energy will result in reactions is also increased. A functional relationship is found to exist between $A$ and $E$.

IN Part I (Newitt, Linstead, Sapiro, and Boorman, J., 1937, 876) it was shown *inter alia* that the rate of esterification of acetic acid with ethyl alcohol was greatly accelerated by increase of hydrostatic pressure; *e.g.*, at 6500 atm. the system passes more than half-way to equilibrium under conditions which give only a very small amount of esterification at atmospheric pressure.

The effect of pressure upon a similar esterification, *viz.*, that of acetic anhydride with ethyl alcohol in dilute alcoholic and toluene solutions, severally, has been investigated by Williams, Perrin, and Gibson (*Proc. Roy. Soc.*, 1936, *A*, **154**, 684), who also observed a marked increase in the rate of reaction with pressure; by applying the reaction-velocity equation $k = PZe^{-E/RT}$ to their results ($Z$ being evaluated by the gas collision formula), they showed that the experimental value of the velocity constant is several powers of ten less than the calculated value. In conformity with all other "slow" reactions in like circumstances, the pressure effect in toluene solution is to cause an apparent increase in the activation energy, $E$, and a more than compensating increase in the value of the product $PZ$. In alcoholic solution, on the other hand, both $E$ and $PZ$ decrease with increasing pressure although the net effect of pressure on the rate is of the same order as in the toluene solution; they suggest that "some complicating factor due to the effect of pressure on the collision rate" may afford an explanation of this difference in behaviour.

In this connexion it may be pointed out that some uncertainty attaches to the value of the collision number $Z$ in the case of liquid-phase reactions; if the gas-kinetic value is accepted then the probability factor $P$ is found to vary from reaction to reaction between the limits 1 and $10^{-11}$; for a given reaction it may also vary from solvent to solvent or with change of hydrostatic pressure. There is, moreover, reason to believe that collisions between pairs of molecules of different species, leading to interaction in dilute solution, are of a special kind, differing not only from those in the gas-phase but also from those occurring in a mixture of two miscible liquids in the absence of a solvent (Rabinowitch and Wood, *Trans. Faraday Soc.*, 1936, **32**, 1381). To obtain further information upon these matters we have re-examined in more detail the esterification of acetic acid, and have extended the scope of the earlier work so as to include a series of primary and secondary alcohols. Both in the original experiments and in those described below, only the pure reactants were used, in equimolecular proportions, so that, although the data are unaffected by any purely solvent action other than that arising from the reaction products, they would be expected to show the influence of changes in the compressibility, viscosity, and thermal expansion of the medium due to changes in the hydrostatic pressure.

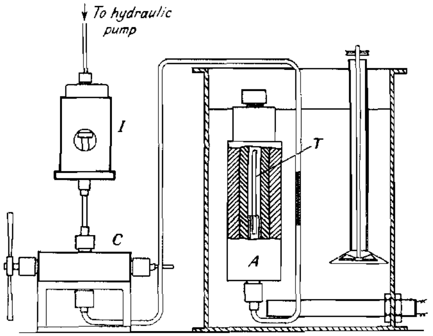
## EXPERIMENTAL.

The method of developing and maintaining hydrostatic pressures of the order of 5000 atm. has been described in Part I (*loc. cit.*). In view of the requirements of the present experiments, however, a rearrangement of the apparatus was necessary (see Fig. 1) in order to enable the reaction vessel to be completely immersed in a constant-temperature bath. The steel reaction vessel, $A$, is connected through the valve $C$ to an intensifier, $I$, by means of which its contents can be raised to the required pressure. The reactants are contained in a glass tube, $T$, over mercury, and pressure is applied through the medium of liquid paraffin, which completely fills the free space in the reaction chamber. In all experiments the pressure was raised at a uniform slow rate to allow sufficient time for the dissipation of the heat of compression.

"AnalaR" Reagents were employed. Acetic acid was recrystallised four times. The alcohols were dried over metallic calcium and subsequently fractionated, through a 3-ft. column,

the fractions distilling within a narrow range of the accepted b. p.'s being collected. The mercury was purified by agitation with dilute nitric acid, washing with distilled water, and distillation in a vacuum.

FIG. 1.




The glass reaction vessels were treated with warm chromic acid, followed by repeated washings with distilled water. As there is a possibility of some solvent action on the glass at high pressures resulting in catalytic action, a number of comparative experiments were carried out in glass and transparent silica vessels of the same linear dimensions. In no case was any appreciable difference in the rate of esterification observed; *e.g.*, in the esterification of acetic acid with *n*-propyl and *n*-butyl alcohol, respectively, the following data were obtained:

| | Values of $k \times 10^7$ at 80° from experiments in (1) a glass vessel. | (2) a silica vessel. |
|---|---|---|
| *n*-Propyl alcohol | 131·5 | 135·9 |
| *n*-Butyl alcohol | 128·8 | 127·0 |

The agreement is well within the experimental error.

The initial acid–alcohol mixtures were made up hy weight immediately before each experiment. The percentage esterification was determined by titration of the free acid, followed by hydrolysis of the ester with an excess of standard alkali. The velocity constants, *k*, were calculated from the simple bimolecular expression, corrections being made for the changes in concentration due to the compressibilities and thermal expansions of the reactants. For the various alcohols, Bridgman's compressibility data were employed; for acetic acid no data are available, and in order to make the correction a value intermediate between that of ethyl alcohol and ethyl acetate has been assumed.

In the tabulated results (Table I) the corrected values of *k* are given in the units l./g.-mol.-sec.

The constants for the *n*-primary alcohols are all of the same order, tending, if anything, to diminish as the series is ascended; *iso*propyl and *sec.*-butyl alcohols have comparatively low constants, but those of *iso*butyl alcohol, which contains the primary $-CH_2OH$ group, are high. In Fig. 2, $\log_{10}k-1/T$ isobars for the various alcohols at 3000 atm. are shown, together with (inset) isobars for ethyl alcohol at 1, 2000, 3000, and 4000 atm. In all cases a satisfactory linear relationship is exhibited.

The effect of pressure ($k_p/k_1$) is most marked in the case of ethyl and *sec.*-butyl alcohols, and is least so for *iso*butyl alcohol; for the primary alcohols $k_{8750}/k_1$ diminishes on ascending the series from 17·9 for ethyl alcohol to 12·8 for *n*-butyl alcohol. In general, the order of the effect is greater than for reactions of the same type in dilute solution; *e.g.*, according to Williams, Perrin, and Gibson (*loc. cit.*), $k_p/k_1$ for the esterification of acetic anhydride with ethyl alcohol in toluene solution, at 30° and over the same pressure range, is only about 2. It will also be observed that the pressure effect shows a slight but definite increase with increase of temperature.

TABLE I.

*Velocity Constants for the Esterification of Acetic Acid with a Series of Alcohols at Pressures between 1 and 4000 Atmospheres.*

| | Pressure, atm. | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 1. | 2000. | | 3000. | | 3750. | | 4000. | |
| Temp. | $k_1 \times 10^7$. | $k_p \times 10^7$. | $k_p/k_1$. | $k_p \times 10^7$. | $k_p/k_1$. | $k_p \times 10^7$. | $k_p/k_1$. | $k_p \times 10^7$. | $k_p/k_1$. |
| | | | | Ethyl alcohol. | | | | | |
| 50° | 2·34 | 12·35 | 5·28 | 25·63 | 10·9 | — | — | 60·01 | 25·7 |
| 60 | 4·20 | 20·88 | 4·97 | 47·92 | 11·4 | — | — | 101·35 | 23·6 |
| 70 | 7·98 | 41·42 | 5·19 | 81·30 | 10·2 | — | — | 193·80 | 24·2 |
| 75 | 12·70 | 58·10 | 5·33 | 125·00 | 11·5 | 227·5 | 17·9 | — | — |
| | | | | *n*-Propyl alcohol. | | | | | |
| 70 | 10·04 | 41·80 | 4·14 | 81·30 | 8·10 | 136·00 | 13·5 | | |
| 75 | 13·28 | 56·22 | 4·23 | 108·40 | 8·16 | 182·40 | 13·7 | | |
| 80 | 17·82 | 77·05 | 4·32 | 144·60 | 8·11 | 254·00 | 14·2 | | |
| | | | | *n*-Butyl alcohol. | | | | | |
| 70 | 10·41 | 37·20 | 3·58 | 74·20 | 7·14 | 123·0 | 11·8 | | |
| 75 | 13·07 | 51·88 | 3·97 | 100·40 | 7·70 | 167·0 | 12·8 | | |
| 80 | 17·27 | 73·70 | 4·28 | 145·20 | 8·42 | 226·0 | 13·1 | | |
| | | | | *iso*Propyl alcohol. | | | | | |
| 70 | 2·44 | 9·37 | 3·84 | 18·59 | 7·62 | 30·84 | 12·6 | | |
| 75 | 3·31 | 14·13 | 4·37 | 28·84 | 8·72 | 49·10 | 14·8 | | |
| 80 | 4·40 | 20·97 | 4·76 | 44·26 | 10·10 | 77·80 | 17·7 | | |
| | | | | *iso*Butyl alcohol. | | | | | |
| 70 | 20·55 | 53·98 | 2·63 | 86·10 | 4·29 | 128·2 | 6·25 | | |
| 75 | 28·19 | 77·69 | 2·72 | 131·20 | 4·66 | 191·6 | 6·70 | | |
| 80 | 39·20 | 116·00 | 2·96 | 188·40 | 4·81 | 279·7 | 7·09 | | |
| | | | | *sec.*-Butyl alcohol. | | | | | |
| 70 | 1·77 | 9·68 | 5·46 | 20·66 | 11·65 | 36·22 | 20·45 | | |
| 75 | 2·68 | 14·13 | 5·27 | 31·75 | 11·85 | 57·60 | 21·50 | | |
| 80 | 3·89 | 21·14 | 5·44 | 49·20 | 12·64 | 90·50 | 23·30 | | |

From the data in Table I the values of the activation energy, $E$, and the constant, $A$, of the Arrhenius equation ($k = Ae^{-E/RT}$) for the various pressures have been calculated and are summarised in Table II. For all the reactions studied both $E$ and $A$ increase with pressure,

TABLE II.

*Values of the Constants of the Arrhenius Equation for the Rate of Esterification of Acetic Acid with a Series of Alcohols.*

| Alcohol. | Press., atm. | $E$, cals. | $A$ or $PZ$. | Alcohol. | Press., atm. | $E$, cals. | $A$ or $PZ$. |
|---|---|---|---|---|---|---|---|
| Ethyl | 1 | 13,770 | $4{\cdot}58 \times 10^2$ | *iso*Propyl | 1 | 15,890 | $3{\cdot}20 \times 10^3$ |
| | 2000 | 13,790 | $2{\cdot}40 \times 10^3$ | | 2000 | 19,400 | $2{\cdot}15 \times 10^6$ |
| | 3000 | 13,830 | $6{\cdot}10 \times 10^3$ | | 3000 | 20,680 | $2{\cdot}66 \times 10^7$ |
| | 4000 | 13,980 | $1{\cdot}61 \times 10^4$ | | 3750 | 22,220 | $4{\cdot}38 \times 10^8$ |
| *n*-Propyl | 1 | 13,550 | $4{\cdot}10 \times 10^2$ | *iso*Butyl | 1 | 16,480 | $4{\cdot}84 \times 10^4$ |
| | 2000 | 13,910 | $2{\cdot}98 \times 10^3$ | | 2000 | 17,850 | $1{\cdot}30 \times 10^6$ |
| | 3000 | 14,190 | $8{\cdot}87 \times 10^3$ | | 3000 | 18,240 | $3{\cdot}35 \times 10^6$ |
| | 3750 | 14,740 | $3{\cdot}33 \times 10^4$ | | 3750 | 18,780 | $1{\cdot}16 \times 10^7$ |
| *n*-Butyl | 1 | 13,720 | $5{\cdot}69 \times 10^2$ | *sec.*-Butyl | 1 | 17,460 | $2{\cdot}50 \times 10^4$ |
| | 2000 | 14,580 | $7{\cdot}00 \times 10^3$ | | 2000 | 19,790 | $3{\cdot}53 \times 10^6$ |
| | 3000 | 14,950 | $2{\cdot}44 \times 10^4$ | | 3000 | 21,010 | $4{\cdot}90 \times 10^7$ |
| | 3750 | 15,190 | $5{\cdot}72 \times 10^4$ | | 3750 | 21,720 | $2{\cdot}22 \times 10^8$ |

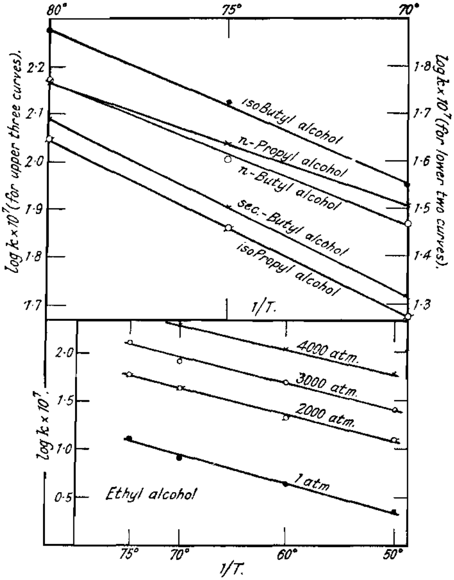
the effect being greatest with *iso*propyl and *sec.*-butyl alcohols; the activation energies of the *n*-primary alcohols increase progressively on ascending the series at all pressures above atmospheric.

## DISCUSSION.

If the constant $A$ be identified with the product of the collision number, $Z$, and a probability factor, $P$, then, provided the value of the former be known with some degree of certainty at the various pressures, we can obtain, through the latter, a measure of the collision efficiency and the effect of pressure thereon. There is much evidence to suggest

that the frequency of binary collisions in the liquid phase is greater than in the gas phase; for instance, Evans and Polanyi (*Trans. Faraday Soc.*, 1936, **32**, 1350) relate the two frequencies through the entropies of solution of the reactants and the transition state and find log $Z_{sol.}/Z_{gas} \sim 3$ to 2; the value of $Z$ calculated from the diffusion coefficient and the "free space" of the liquid according to Jowett's hypothesis (*Phil. Mag.*, 1929, **8**, 1059) is $10^{14}$; and a value of the same order is given by Bradley's equation (*Trans. Faraday Soc.*, 1937, **33**, 1185), which is also based upon the diffusion coefficient.

Fig. 2.




We may therefore assume that the collision frequency in the liquid phase is about $10^3$ times that in the gas phase under comparable conditions. If we follow Jowett's derivation, the effect of increased hydrostatic pressure will be to increase $Z$ approximately in proportion to the increase of viscosity of the medium. In the case of reactions occurring in dilute solutions, the viscosity of the solvent only will be concerned; in our experiments, on the other hand, it is the viscosity of the reactants that matters, and unfortunately no data are available for the pressure coefficients of viscosity of the mixtures concerned. For pure liquids the coefficient varies considerably even amongst related compounds, as may be seen from the following values for a series of alcohols:

*Pressure Coefficient of Viscosity* ($\eta_p/\eta_1$) *for Alcohols at* 75° (*Bridgman*).

| Substance. | | EtOH. | PrOH. | BuOH. | Pr$^{\beta}$OH. | Bu$^{\beta}$OH. |
|---|---|---|---|---|---|---|
| $p$, kg./cm.$^2$ | 1000 | 1·65 | 1·92 | 2·11 | 2·22 | 2·40 |
| | 2000 | 2·44 | 3·00 | 3·50 | 3·83 | 4·30 |
| | 4000 | 4·29 | 5·89 | 7·30 | 8·39 | 11·00 |

If we adopt the value $\eta_{3750}/\eta_1 = 10$ for all the mixtures, then it follows from the data in Table II that at atmospheric pressure the probability factor for the *n*-primary alcohols is approximately $10^{-12}$ and for the *iso*- and *sec*.-alcohols is between $10^{-11}$ and $10^{-10}$; at 3750 atm. it has increased by a factor of 10 for the former and by $10^3$—$10^4$ for the latter. Comparing these values with the corresponding figures for typical " normal " and " slow " reactions in dilute solution (Williams, Perrin, and Gibson, *loc. cit.*), we note that whilst for most " normal " reactions the probability factor is about 1 and does not appreciably alter with pressure, yet for " slow " reactions it is of the order of $10^{-6}$ and the variation with pressure may be comparatively large and may be either positive or negative in sign. The data given below for the esterification of acetic anhydride with ethyl alcohol (1) in solution in large excess of the alcohol, and (2) in solution in toluene, serve to show the order of the effect:

*Values of the Constant* P $\times$ $10^6$ *for the Rate of Esterification of Acetic Anhydride with Ethyl Alcohol.*

| Pressure, kg./cm.². | (1) In ethyl-alcoholic soln. | (2) In toluene soln. |
|---|---|---|
| 1 | 38·5 | 1·3 |
| 3000 | 0·677 | 8·5 |

It is evident that the efficiency of collisions between reactant molecules is increased by the presence of a solvent, or conversely, that a molecule has a greater chance of losing its energy of activation by collision with other reactant molecules than by collision with solvent molecules.

*The Effect of Pressure upon the* E *Term of the Arrhenius Equation.*—It seems very improbable that the true activation energy of a bimolecular reaction will increase with pressure to anything like the extent that $E$ is found to increase; $E$ is, in fact, a composite term made up of various energy contributions, some of which are due to changes in the physical properties of the medium, and are, therefore, dependent on the pressure. Of these mention may be made of the activation energy of diffusion (Rabinowitch, *Trans. Faraday Soc.*, 1937, **33**, 1225; Bradley, *loc. cit.*), the increase of the activation energy due to the positive temperature coefficient of the collision rate (or viscosity), and the energy associated with any change in volume accompanying the formation of activated or transition complexes (Moelwyn-Hughes, *Trans. Faraday Soc.*, 1936, **32**, 1725; Evans and Polanyi, *ibid.*, 1937, **33**, 448). Unfortunately, the data required for the calculation of the value of these contributions are seldom available, and only in a few instances is it possible to obtain some idea of their relative magnitudes.

From measurements of the diffusion velocity of hydrogen peroxide in water (Stern, *Ber.*, 1933, **66**, 547), and from other considerations, it is probable that the activation energy of diffusion of liquids of the type of aliphatic alcohols and acids is of the order of 3000 cals. It has also been found that for a large number of liquids, the increase of activation energy due to the change in viscosity, as the temperature is raised, is 1500—3000 cals.

Attention may also be directed to the difference in the activation energies calculated from the temperature coefficients of the velocity constants as measured severally at constant volume and at constant pressure. The two coefficients are related by the expression

$$\left(\frac{\partial \log k}{\partial T}\right)_v = \left(\frac{\partial \log k}{\partial T}\right)_p + \left(\frac{\partial \log k}{\partial p}\right)_T \left(\frac{\partial p}{\partial V}\right)_T \left(\frac{\partial V}{\partial p}\right)_p$$

and it has been shown (Evans and Polanyi, *Trans. Faraday Soc.*, 1935, **31**, 875) that over a pressure range of 3000 atm. the difference may amount to upwards of 10%.

The energy associated with the formation of an activated or transition complex is more difficult to determine. Moelwyn-Hughes (*loc. cit.*), for example, deduces the following expression for the velocity constant, on the assumption that the reaction velocity is proportional to the number of molecules (or complexes) for which the free energy, $F$, has reached a certain critical value:

$$k = \text{constant} \times e^{-\Delta F^*/RT}$$

where $$\Delta F = \Delta E + P\,\Delta V - T\,\Delta S$$

Evans and Polanyi (*loc. cit.*), also by means of a semi-thermodynamical treatment, show that the change in the velocity constant with pressure may be calculated from the equation

$$\partial \log_e k/\partial\pi = (V_1 - V_t)/\mathbf{R}T$$

where $V_t$ is the molar volume of the transition state. The change in the activation energy with pressure is then given by

$$E_a = E_0 + \pi(V_1 - V_t)\{1 - T[\partial \log_e (V_1 - V_t)/\partial T]_\pi\}$$

where $E_0$ is the value of $E_a$ for $\pi = 0$. From our results the values of $(V_1 - V_t)$ have been calculated and are tabulated below.

*Values of* $(V_1 - V_t)$, *c.c.*

| Alcohol. Temp. | 50°. | 60°. | 70°. | 75°. | 80°. |
|---|---|---|---|---|---|
| Ethyl | 21·5 | 22·45 | 22·48 | 23·35 | — |
| *n*-Propyl | — | — | 19·70 | 20·03 | 20·39 |
| *n*-Butyl | — | — | 18·44 | 18·94 | 19·50 |
| *iso*Propyl | — | — | 18·90 | 20·45 | 21·47 |
| *iso*Butyl | — | — | 13·70 | 14·23 | 14·84 |
| *sec.*-Butyl | — | — | 22·20 | 22·00 | 24·40 |

On plotting log $k_p/k_0$ against pressure, a series of nearly straight lines (Fig. 3) is obtained, indicating that for the pressure range 1—4000 atm. the volume change $(V_1 - V_t)$ is substantially independent of the pressure. Our results, however, do not enable us to calculate the variation of this quantity with temperature at constant pressure, and hence $E_0$ cannot be evaluated.

Fig. 3.

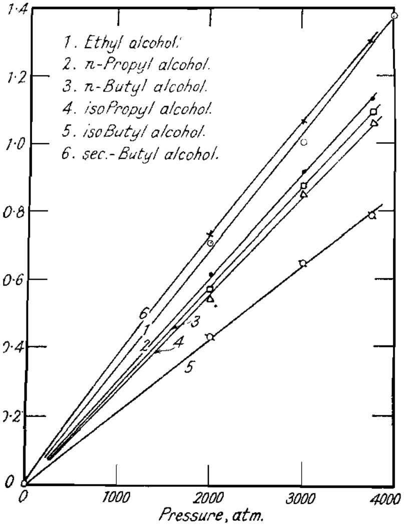
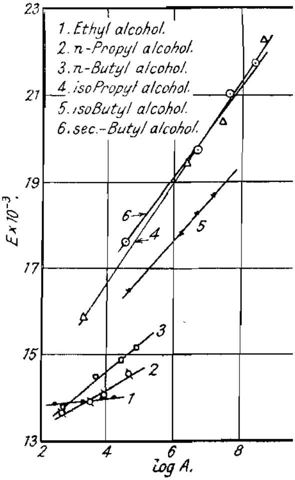



Fig. 4.




*The Functional Relationship between* A *and* E.—Since both $A$ and $E$ contain terms which are functions of pressure, we should expect a simple relationship to exist between the values of log $A$ and $E$, calculated from the reaction-velocity constants determined over

a range of pressures for any given reaction. That such is the case may be seen from Fig. 4, in which a linear relationship is found to hold for all the reactions.

A similar correlation of $A$ and $E$ has been observed for reactions in which the pressure is maintained constant but the solvent is altered; and Fairclough and Hinshelwood (J., 1937, 538) have shown that it should hold for all reactions in which the lifetime of the activated complex (the formation of which is a prelude to reaction) is less than the time taken for the internal vibrations of the molecules to attain the right phase for reaction; their theoretical treatment indicates that log $A$ should be proportional to $1/\sqrt{E}$.

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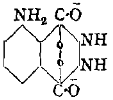
## 151. *Chemiluminescent Organic Compounds. Part VI. The Isolation of Peroxide Derivatives of Phthalaz-1 : 4-diones.*

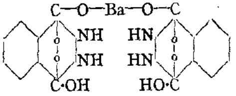
By H. D. K. DREW and R. F. GARWOOD.

Crystalline compounds of the salts of several phthalaz-1 : 4-diones and hydrogen peroxide have been isolated. They have chemiluminescent properties and are probable intermediates in the luminescing reactions of the diones. The diones appear to act as vehicles, bringing hydrogen peroxide into a condition in which it can be oxidised with chemiluminescence. By the use of duroquinol, atmospheric oxygen may be employed in the chemiluminescent reactions of the diones.

A SOLUTION of the sodium salt of 5-aminophthalaz-1 : 4-dione in aqueous hydrogen peroxide gave, on precipitation with alcohol, a crystalline *peroxide*, which was shown by analysis to have the composition of a monohydrate of the sodium salt of the dione with a molecular proportion of hydrogen peroxide. The water molecule could be removed with little loss of hydrogen peroxide. When dissolved in water, the peroxide gave a bright luminescence with hæmoglobin or a copper salt as catalyst; the luminescence was enhanced by addition of more alkali. The aqueous solution of the peroxide gave the unchanged dione when precipitated with acetic acid; mineral acids likewise set free the hydrogen peroxide, and in water alone the peroxide appeared to be in equilibrium with its constituents.

Other considerations had already led us to suppose (J., 1937, 1843) that a peroxide of the above composition would be found as an intermediate in the chemiluminescent reactions of this series, and we had assigned to the ion the provisional formula (I). Since, however, amino-compounds sometimes form complexes in which hydrogen peroxide is apparently associated with the amino-group, attempt was made to see whether this might not be the case in the present instance. Phthalaz-1 : 4-dione, which contains no amino-group, was substituted for the former dione, and the peroxide of the *barium* salt was obtained in a fairly pure condition. This substance contained about two molecular proportions of hydrogen peroxide to one of the barium salt of the dione (II). It seems certain, therefore, that the hydrogen peroxide molecules are not associated with the phenyl groups of the diones, and they are thus probably in combination with the hydrazide rings. Although the structures must still be regarded as provisional, the alternatives are now few and none of them seems to offer so satisfactory an interpretation of the chemiluminescence.

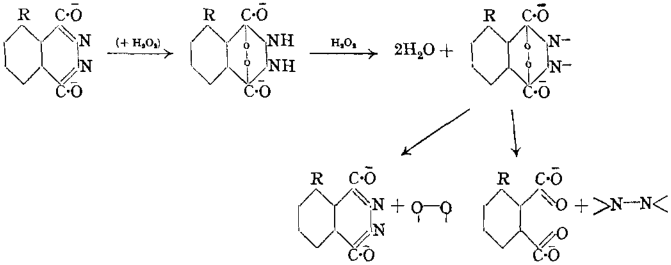
(I.) 


 (II.)


Other salts of the foregoing diones, and also salts of other diones, have been shown to afford peroxide derivatives of the like character, although they have not yet been obtained pure.

When phthalaz-1 : 4-dione is oxidised with sodium hypochlorite, it gives benzophenone-

*oo'*-dicarboxylic acid (Zellner and Dougherty, *J. Amer. Chem. Soc.*, **1937**, **59**, 2580). We confirmed this observation, but found that, when the oxidation with sodium hypochlorite was conducted in the presence of a constant excess of hydrogen peroxide, phthalic acid only was produced; 5-nitrophthalaz-1 : 4-dione similarly give 3-nitrophthalic acid. In the absence of hydrogen peroxide, phthalaz-1 : 4-dione gave the theoretical volume of nitrogen on oxidation with sodium hypochlorite, and 5-aminophthalaz-1 : 4-dione gave under the same conditions the whole of the nitrogen of the hydrazide ring and about two-fifths of that of the amino-group. When, however, an aqueous solution of the sodium salt of 5-aminophthalaz-1 : 4-dione (1 mol.), containing hydrogen peroxide (10 mols.), was treated slowly with sodium hypochlorite (2·5 mols.), with shaking, there was continuous chemiluminescence, but only about one-seventh of the hydrazide nitrogen was liberated. This, and other similar experiments, indicate that the dione is not necessarily oxidised in the chemiluminescent reaction, but rather enters into peroxide formation and is then released by the oxidation of the imino-hydrogen atoms of the peroxide. The dione thus may act as a vehicle for the oxidation of hydrogen peroxide by the same or by another oxidising agent (in this instance, the hypochlorite). Catalysts, such as hæmoglobin or copper salts, facilitate the latter oxidation, especially when hydrogen peroxide is the oxidising agent; but they do not influence the formation of the complex peroxide ion of the dione. The following sequence of reactions may thus be pictured during the chemiluminescent interaction between a dione and hydrogen peroxide:




Radiation of light will probably occur chiefly after the release of oxygen as shown on the left of the final stage, but the other scheme is not excluded. At the ordinary temperature and in the absence of catalysts, hydrogen peroxide is capable of oxidising the dione peroxide only very slowly, but other oxidising reagents are evidently more effective. Oxidising agents which produce a chemiluminescence with the diones in the absence of hydrogen peroxide may be regarded as generators of hydrogen peroxide from water molecules under alkaline conditions.

It has been shown in a number of cases of bioluminescence that atmospheric oxygen acts as the oxidising agent, in the presence of an enzyme functioning as a catalyst. We now find that atmospheric oxygen can be used also in the cases of several of the diones, if duroquinol (*e.g.*, in solution in alcohol) be added. An alkaline solution of 5-aminophthalaz-1 : 4-dione gives in this way a feeble glow when aërated in the absence of a catalyst, but a strong glow when hæmoglobin is added. James and Weissberger (*J. Amer. Chem. Soc.*, 1938, **60**, 98) have shown that duroquinol interacts with oxygen molecules at normal temperatures to give hydrogen peroxide and the quinone. The action of this and other quinols in promoting chemiluminescence, in conjunction with reducing mechanisms, is being studied.

EXPERIMENTAL.

*Sodium Salt of 5-Amino-1 : 4-dihydroxy-2 : 3-dihydrophthalazine Peroxide.*—The dione (1 g.) was dissolved in 5% aqueous sodium hydroxide (about 5 c.c.; 1 mol.), the solution cooled,

and perhydrol (30% strength; 5 c.c.) added. After a time, the mixture was treated with about 20 c.c. of alcohol (96%), and cooled to 0°; small, very faintly yellow needles of the *sodium* salt of the *peroxide monohydrate* separated, and were filtered off, washed with alcohol and ether, and dried on porous tile in a vacuum over calcium chloride. After ½—4 hours, the product was analysed for peroxide oxygen and simultaneously by combustion for the remaining elements [Found: C, 38·3; H, 4·0; N, 17·1; Na, 9·2; O (by diff.), 31·4; $H_2O_2$ (observed), 11·4. $C_8H_8O_4N_3Na,H_2O$ requires C, 38·25; H, 4·0; N, 16·75; Na, 9·15; O, 31·85; $H_2O_2$, 13·55%]. The peroxide only slowly lost hydrogen peroxide in air; it was readily soluble in water, in which it was partly dissociated; in a vacuum over phosphoric oxide it lost the water molecule, without much loss of hydrogen peroxide, but at 120° the hydrogen peroxide also was lost. An aqueous solution of the peroxide gave the pure dione almost quantitatively when acidified with acetic acid (Found: dione, 69·6. Calc., 70·4%). The hydrogen peroxide estimation was carried out with potassium iodide and dilute sulphuric acid, in presence of ammonium molybdate as catalyst, according to a standard procedure; blank tests showed that 5-aminophthalaz-1 : 4-dione did not interfere with the estimation, but we are inclined to think that the amino-group of the peroxide was responsible for the low result obtained for the peroxide oxygen as compared with the result from the elementary analysis.

Peroxides of the potassium and barium salts of 5-aminophthalaz-1 : 4-dione have been obtained, but so far without the full content of hydrogen peroxide.

*Barium Salt of* 1 : 4-*Dihydroxy*-2 : 3-*dihydrophthalazine Peroxide.*—The sodium salt of the dione was treated, as described above, with perhydrol, the solution kept at 0° for 2 hours and filtered from a trace of precipitate, and the filtrate treated with an aqueous solution of barium chloride (1 mol.) containing the same proportion of hydrogen peroxide as the former solution: the precipitated *barium* salt was dried on a porous tile in air for a day and analysed as above [Found: C, 36·3; H, 3·05; Ba, 26·0; N (calc. on carbon), 10·5; O (by diff.), 24·15; $H_2O_2$ (observed), 8·6. $C_{16}H_{14}O_8N_4Ba$ requires C, 36·4; H, 2·65; Ba, 26·05; O, 24·3; N, 10·6; $H_2O_2$, 12·9%]. The peroxide is very sparingly soluble in water; it appears to be fairly stable in air.

The authors thank the Department of Scientific and Industrial Research for a grant.

QUEEN MARY COLLEGE (UNIVERSITY OF LONDON), E. 1. [*Received, March 30th*, 1938.]

## 152. *New Ethylidene Compounds of α- and β-Methylglucosides.*

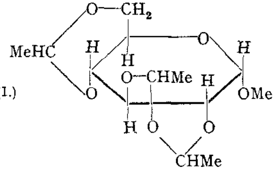
By HERBERT APPEL, W. N. HAWORTH, and (in part) E. G. COX and F. J. LLEWELLYN.

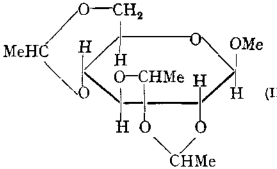
α- and β-Methylglucosides give, on treatment with paraldehyde and concentrated sulphuric acid, triethylidene compounds, which are shown to be 2 : 3-*oxidodiethylidene* 4 : 6-*ethylidene-α-* and -*β-methylglucosides*. A 2 : 3-*oxidodiethylidene* 4 : 6-*benzylidene α-methylglucoside* has also been prepared. The monoethylidene α-methylglucoside obtained by Hibbert and Hill (*J. Amer. Chem. Soc.*, 1923, **45**, 3115) is found to be 4 : 6-ethylidene α-methylglucoside. *X*-Ray data for these compounds are recorded, and the bearing of the results on the question of the conformation of the pyranose ring discussed.

IT has long been known that α- and β-methylglucosides combine with benzaldehyde to form 4 : 6-benzylidene compounds; more recently, furfural (Bredereck, *Ber.*, 1935, **68**, 777, 2299) and acetaldehyde have been shown to react in the same manner as benzaldehyde. Hibbert and Hill (*J. Amer. Chem. Soc.*, 1923, **45**, 3115; cf. Hill, *ibid.*, 1928, **50**, 2729) obtained 4 : 6-ethylidene α-methylglucoside by the action of acetylene on a solution of α-methylglucoside in glycol containing mercuric sulphate and sulphuric acid; the structural formula was assigned only by analogy with the benzylidene compounds. The structure of 4 : 6-ethylidene β-methylglucoside was later proved by Helferich and Appel (*Ber.*, 1931, **64**, 1841), who prepared it by shaking β-methylglucoside with paraldehyde and a trace of concentrated sulphuric acid.

The method of Helferich and Appel leads, however, under suitable conditions to ethylidene derivatives of α- and β-methylglucosides of a hitherto unknown type. The

experimental evidence shows that the new substances are 2 : 3-*oxidodiethylidene* 4 : 6-*ethylidene-α-* (I) and -β-*methylglucosides* (II). The percentages of carbon and hydrogen in

(I.) 

 (II.)

a diethylidene methylglucoside are very close to those in an oxidodiethylidene ethylidene methylglucoside, but accurate determination of the molecular weight of the oxidodiethylidene ethylidene α-methylglucoside by the *X*-ray method (E. G. C. and F. J. L.) and also the acetaldehyde determinations leave no doubt about the empirical formulæ of the new substances.

In order to decide on the structure of the new compounds it was necessary to establish the constitution of the monoethylidene α-methylglucoside of Hibbert and Hill (*loc. cit.*). This was done by the method which Helferich and Appel (*loc. cit.*) used to prove the structure of 4 : 6-ethylidene β-methylglucoside. The compound was methylated with methyl iodide and silver oxide, and the resulting syrup treated with benzaldehyde and zinc chloride. 4 : 6-Benzylidene 2 : 3-dimethyl α-methylglucoside was obtained and the assumption of Hibbert and Hill was therefore correct. Attention may be drawn to the fact that the melting point of 4 : 6-ethylidene α-methylglucoside (77°) is about 100° lower than the melting points of all corresponding compounds. When oxidodiethylidene ethylidene-α (or β)-methylglucoside is boiled for a few minutes with ether containing a few drops of bromine, 4 : 6-ethylidene-α (or β)-methylglucoside is formed (the probable reason for the hydrolysis is the small amount of hydrogen bromide present). This reaction affords evidence that two molecules of acetaldehyde are involved in a link between the atoms $C_2$ and $C_3$ of the glucose chain. It also shows the great lability of the new ring system towards acids.

It was further possible to obtain 2 : 3-oxidodiethylidene 4 : 6-benzylidene α-methylglucoside from 4 : 6-benzylidene α-methylglucoside by treatment with paraldehyde and concentrated sulphuric acid. This substance and 2 : 3-oxidodiethylidene 4 : 6-ethylidene α-methylglucoside have molecular rotations of 23,400° and 24,200° respectively, suggesting that the two substances agree not only in structure but also in configuration.

It is to be expected that the new type of oxidodiethylidene ring may also be formed with other compounds having two hydroxyl gronps at a suitable distance. Such substances may be *trans-cyclo*hexane-1 : 2-diol and *cis-cyclo*hexane-1 : 3-diol; it is intended to test this hypothesis.

## Experimental.

2 : 3-*Oxidodiethylidene* 4 : 6-*Ethylidene α-Methylglucoside.*—α-Methylglucoside (1·0 g.) was shaken for several hours with a mixture of paraldehyde (10 c.c.) and concentrated sulphuric acid (2 drops). Chloroform was then added, and the clear solution was treated with solid potassium carbonate for a few minutes and filtered. The solvent was removed under diminished pressure, and the residue recrystallised from alcohol or ligroin. Yield, 0·8 g.; m. p. 182·5—183·5°, $[\alpha]_D^{20°}$ +83·5° in chloroform [Found: C, 53·9; H, 7·85; *M*, by *X*-ray method (see p. 796), 288 ± 5; *M*, cryoscopic in benzene, 266. (All the molecular weights determined by the cryoscopic method in benzene were found to be somewhat low, but tetra-acetyl β-methylglucoside also gave in a test experiment a molecular weight of 339 instead of the calculated 362.) 2 : 3-*Oxidodiethylidene* 4 : 6-*ethylidene α-methylglucoside*, $C_{13}H_{22}O_7$, requires C, 53·8; H, 7·6%; *M*, 290. Calc. for a diethylidene methylglucoside, $C_{11}H_{18}O_6$: C, 53·6; H, 7·4%; *M*, 246].

2 : 3-*Oxidodiethylidene* 4 : 6-*Ethylidene β-Methylglucoside.*—β-Methylglucoside (1·0 g.) was shaken with a mixture of paraldehyde (10 c.c.) and concentrated sulphuric acid (1 drop) for 6

ys (the time is probably unnecessarily long; 2 days should suffice). The reaction mixture is worked up as described above. The *product*, recrystallised from alcohol, had m. p. 208—19° and $[\alpha]_D^{21°}$ −57·8° in chloroform (Found : C, 53·7; H, 7·6%; *M*, in benzene, 260).

*Acetaldehyde determinations.* A weighed amount of the compound was boiled for 15—20 inutes with 2% sulphuric acid. The acetaldehyde was distilled into ice-cooled water and etermined in the solution by means of dimedone (Vörlander, *J. pr. Chem.*, 1929, **77**, 321). xidodiethylidene ethylidene-α- and -β-methylglucoside gave 41·8 and 42·2% respectively of cetaldehyde (Calc., 45·5%. Calc. for a diethylidene methylglucoside, 35·8%).

2 : 3-*Oxidodiethylidene* 4 : 6-*Benzylidene* α-*Methylglucoside.*—4 : 6-Benzylidene α-methyl-lucoside (m. p. 165°; 3·6 g.) was shaken with a mixture of paraldehyde (37 c.c.) and oncentrated sulphuric acid (4 drops). After 8 minutes the clear solution was diluted with enzene, washed at once with sodium carbonate solution and water, and dried with calcium hloride. The solvent was removed under diminished pressure. The residue was dissolved n methyl alcohol, and water added until no further crystalline material separated. The crystals 0·55 g.) were filtered off from the solution (A) and recrystallised several times from alcohol; n. p. 192—193°; $[\alpha]_D^{20.5°}$ +66·4° in chloroform (Found : C, 61·5; H, 6·9; OMe, 9·2; *M*, in enzene, 333. 2 : 3-*Oxidodiethylidene* 4 : 6-*benzylidene* α-*methylglucoside*, $C_{18}H_{24}O_7$, requires C, 61·3; H, 6·9; OMe, 8·8%; *M*, 352·2. Calc. for a monoethylidene benzylidene methyl-glucoside, $C_{16}H_{20}O_6$ : C, 62·3; H, 6·5; OMe, 10·1%; *M*, 308·2). The solution (A) contained oxidodiethylidene α-methylglucoside.

4 : 6-*Ethylidene* α-*Methylglucoside.*—(a) Conditions are described here which permit the preparation of a certain amount of this compound from α-methylglucoside directly by the paraldehyde method. The hydrolysis of oxidodiethylidene ethylidene α-methylglucoside [see (b)] is, however, more satisfactory.

α-Methylglucoside (1·0 g.) was shaken with a mixture of paraldehyde (10 c.c.) and concentrated sulphuric acid (1 drop) for 1 hour. Chloroform was added and the mixture, which contained undissolved material, was treated with solid potassium carbonate, filtered, and the solvent removed in a vacuum. The residue was dissolved in slightly alkaline water, leaving a residue (0·2 g.) of oxidodiethylidene ethylidene α-methylglucoside. The aqueous solution was evaporated to dryness, and the product extracted with hot ether. The ethereal solution contained 4 : 6-ethylidene α-methylglucoside (about 0·1 g.), which was recrystallised by careful addition of light petroleum to a solution in carbon tetrachloride; m. p. 77°, $[\alpha]_D^{20°}$ +109·1° in water (Hibbert and Hill, *loc. cit.*, give m. p. 77°, but do not record the rotation) (Found : C, 48·7; H, 7·6. Calc. for $C_9H_{16}O_6$ : C, 49·1; H, 7·3%).

(b) 2 : 3-Oxidodiethylidene 4 : 6-ethylidene α-methylglucoside (1·5 g.) was boiled in ether (100 c.c.) containing a few drops of bromine until the compound had dissolved. The boiling was then continued for a further 3 minutes. An aqueous solution of sodium thiosulphate was added and, when the bromine colour had disappeared, the solution was made alkaline. The ether was evaporated, and 0·4 g. of unchanged starting material removed by filtration. The clear aqueous solution was taken down to dryness, and the residue extracted with hot carbon tetrachloride. After removal of the carbon tetrachloride a syrup (0·95 g.) was obtained which readily crystallised on seeding with 4 : 6-ethylidene α-methylglucoside; m. p., after two recrystallisations from carbon tetrachloride, 76—77°.

4 : 6-*Ethylidene* β-*Methylglucoside.*—2 : 3-Oxidodiethylidene 4 : 6-ethylidene β-methyl-glucoside (0·5 g.) was boiled for about 10 minutes with ether (30 c.c.) containing a few drops of bromine. The product, which began to separate before complete solution had occurred, was filtered off and washed with ether. Yield, 0·3 g.; m. p., after one recrystallisation from acetone, 183—185°; $[\alpha]_D^{19°}$ −76·9° in water [Helferich and Appel, *loc. cit.*, found after about ten recrystallisations m. p. 189—190° (corr.) and $[\alpha]_D$ −79·1°; but a specimen of m. p. 182—183° showed the same rotation and gave correct analytical values (cf. Helferich and Masamune, *Ber.*, 1931, **64**, 1260)].

4 : 6-*Benzylidene* 2 : 3-*Dimethyl* α-*Methylglucoside from* 4 : 6-*Ethylidene* α-*Methyl-glucoside.*—4 : 6-Ethylidene α-methylglucoside (2·0 g.) was dissolved in acetone (8 c.c.), methyl iodide (15 c.c.) added, and the solution boiled on the water-bath for 6 hours. Silver oxide (12 g.) was introduced during this time in three portions; acetone was then added, and the filtered solution evaporated to dryness. The syrup (2·05 g.) was mixed with freshly distilled benzaldehyde (16 c.c.), and zinc chloride (2·5 g.) dissolved with shaking. After 48 hours, the solution was stirred with an aqueous solution of sodium bisulphite until the benzaldehyde had dissolved. The solution was extracted with ether, and the extract washed with sodium bisulphite solution, dilute alkali, and water, and dried with calcium chloride. Removal of the ether left 0·8 g. of

crystalline material, which after recrystallisation from light petroleum showed m. p. 120—121°, not depressed by an authentic specimen (m. p. 120—121·5°); $[\alpha]_D^{25°}$ +96·2° in chloroform (Mathers and Robertson, J., 1933, 698, give m. p. 121—122° and $[\alpha]_D$ +94·6°).

## *Crystallographic Section.*

By E. G. Cox and F. J. Llewellyn.

*X*-Ray studies of carbohydrates (see, *e.g.*, Cox, Goodwin, and Wagstaff, J., 1935, 1495) suggest that the conformation of the pyranose ring in glucose and its derivatives is not, as is frequently assumed, of the Sachse *trans*-type, and the formation of the compounds described in this paper supports this view. Since a five-membered acetal ring must normally be flat, the ease of formation of snch rings between adjacent *cis*-hydroxyl groups in pyranose sugars is difficult to reconcile with a Sachse *trans*-ring, because with such a conformation adjacent C—OH bonds cannot be coplanar. If, in spite of this, the idea of the Sachse *trans*-ring is adhered to, then on account of the symmetrical nature of this ring and the consequent equality of distances between *cis*- and *trans*-pairs of hydroxyl groups, it must be admitted that five-membered ring formation can occur with equal facility whether *trans*- or *cis*-hydroxyl groups are involved. The exceptional seven-membered ring embracing the *trans* $O_2$ and $O_3$ atoms in the compounds now described is in marked contrast with the usual five-membered ring involving *cis*-oxygen atoms, and is in agreement with the view that the pyranose ring in glucose is not of the Sachse *trans*-form.

The length of the *c*-axis for the two oxidodiethylidene ethylidene methylglucosides is almost the same as for 4 : 6-ethylidene α-methylglucoside and for the 4 : 6-benzylidene derivatives (Cox *et al.*, *loc. cit.*); this indicates that the form of the ring is not greatly changed by the addenda in the 2 : 3-position. When a model is made, it is seen that the seven-membered ring is readily formed without strain and lies in approximately the same plane as the remainder of the molecule. It is interesting to note that comparison of the birefringence and cell-dimensions of the four compounds now examined suggests that the molecules of the β-compounds are " flatter " than those of the α-forms. This lends further support to the views previously expressed (Cox *et al.*, *loc. cit.*) regarding the relative configuration of α- and β-derivatives of glucose.

### Experimental.

The *X*-ray data were obtained by means of single crystal rotation and oscillation photographs, using copper $K_\alpha$ radiation. Refractive indices are for sodium light.

4 : 6-*Ethylidene* β-*Methylglucoside.*—The crystals of this substance are monoclinic sphenoidal combinations of *a*{100}, *c*{001}, *R*{10$\bar{1}$}, *m*{1$\bar{1}$0}, and *p*{011}, elongated parallel to [*b*], sometimes tabular on *a* and sometimes on *R*. The dimensions of the unit cell (which contains two molecules) are *a* = 8·58, *b* = 9·56, and *c* = 6·48 A., with β = 112° 54′. The space group is $P2_1$ and the calculated density is 1·40 g./c.c. (obs., 1·40). The refractive indices are α = 1·50 [perp. to *a*(100)], β = 1·52, and γ = 1·56 (parallel to [*b*]). A positive obtuse bisectrix interference figure is visible through *a*(100). The optical results are consistent with the molecules being oriented with their planes approximately parallel to *a*(100), in which case their " thickness " would be *a*/2, *i.e.*, 4·3 A.

4 : 6-*Ethylidene* α-*Methylglucoside.*—Only very small, acicular crystals of this compound could be obtained; they showed straight extinction with negative elongation. By taking a rotation photograph of a bundle of approximately parallel crystals, the unit cell dimension in the needle direction was found to be 4·8 A.

2 : 3-*Oxidodiethylidene* 4 : 6-*Ethylidene* β-*Methylglucoside.*—This substance occurs as minute needles similar to those of the preceding compound, with straight extinction and negative elongation, but having higher birefringence. The length of the needle axis was found to be 4·7 A.

2 : 3-*Oxidodiethylidene* 4 : 6-*Ethylidene* α-*Methylglucoside.*—The crystals of this substance are monoclinic combinations of *a*{100} and *b*{010} elongated parallel to [*c*] and terminated by *m*{011}. [A crop of crystals having a slightly low m. p. (178—179·5°), however, were found to be of pronounced sphenoidal habit, tabular on *a*, with *b*′{0$\bar{1}$0} and *n*{021}. The same type of crystal was sometimes obtained by recrystallisation from carbon tetrachloride.] The unit

cell dimensions are $a = 9.78$, $b = 15.47$, and $c = 4.74$ A., with $\beta = 99° 24'$, and the space-group is $P2_1$. The density (by flotation) is 1·340 g./c.c., so that with two molecules in the unit cell the molecular weight is 288 ± 5 (calc., 290·2). The crystals are optically negative with refractive indices $\alpha = 1.502$ inclined at 3° to [c] in the obtuse angle $\beta$, $\beta = 1.539$ (parallel to [b]), and $\gamma = 1.542$. An obtuse bisectrix interference figure is visible through $a(100)$.

The A. E. Hills Laboratories,
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[Received, April 11th, 1938.]

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# 153. *The Constituents of Natural Phenolic Resins. Part X. Structure of* l-*Matairesinol Dimethyl Ether and Observations on the Condensation of Reactive Methylene Groups with* O-*Methyleugenol Oxide.*

By Robert D. Haworth and John R. Atkinson.

By subjecting *l*-matairesinol dimethyl ether (I; $R^1 = R^2$ = veratryl) to prolonged alkaline treatment, it has been converted into d-iso*matairesinol dimethyl ether*. This *d*-lactone is not the optical antipode of *l*-matairesinol dimethyl ether, but it is rapidly and completely converted into the latter by mild alkaline treatment. It is suggested that these isomerisations involve the asymmetric centre in the α-position with respect to the carbonyl group, that the rapid change from *d-iso-* to *l*-forms occurs without fission of the lactone ring, but the conversion of *l-* into the *d-iso*-form occurs *via* the corresponding hydroxy-acids. The hydroxy-acid corresponding to the *d-iso*-form is lactonised much less readily than the acid from the *l*-isomer, and it is concluded that *d-iso-* and *l*-matairesinol dimethyl ether represent the *cis-* and the *trans*-form respectively of (I; $R^1 = R^2$ = veratryl).

In previous work (J., 1936, 725) a lactone, believed to be structurally identical with *l*-matairesinol dimethyl ether, was prepared by two methods, and improvements have been made in one of the syntheses. The synthetic lactone differs from *d-iso-* and *l*-matairesinol dimethyl ether in crystal structure and in behaviour with lead tetra-acetate and the corresponding hydroxy-acids show wide differences in rates of lactonisation. The differences cannot be accounted for on stereochemical grounds and it is concluded that the synthetic lactone has structure (IV; R = veratryl). This structure has been established by alkaline hydrolysis of the condensation product of ethyl acetoacetate with *O*-methyleugenol oxide; the lactone (VI; $R^1$ = OMe, $R^2$ = H) was obtained and the constitution was proved by an independent synthesis. It follows that lactones previously regarded as α-benzylbutyrolactones are actually γ-benzylbutyrolactones and a list of corrected formulæ is included.

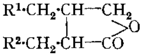
The principle reason for the previous assignation of the α-benzylbutyrolactone structure was based on the facile conversion into naphthalene derivatives. The naphthalene structures have been confirmed, new examples of such conversions are recorded, and it is suggested that the naphthalenes arise from the γ-benzylbutyrolactones by a pinacolinic change during the cyclisation with acidic reagents.

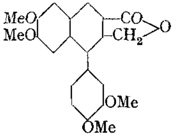
These new observations do not affect previous conclusions with regard to the structure of natural products of the lignan group.

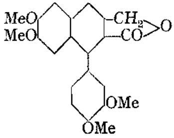
In Part V (J., 1936, 725) the synthesis of a compound believed to be a racemic modification of matairesinol dimethyl ether (I; $R^1 = R^2$ = veratryl) was described. The synthetic product resembles the naturally occurring *l*-lactone in absorption spectra and in its behaviour towards bromine, nitric acid, potassium permanganate, and sodium hypobromite, but the synthetic lactone, unlike the *l*-lactone, could not be converted into the *cyclo*dehydro-lactones (II) and (III) by the action of lead tetra-acetate. A compound of stucture (I) can exist in two racemic (*cis* and *trans*) forms, and in Part V (*loc. cit.*) it was suggested that the inconsistency with lead tetra-acetate might be attributed to stereochemical differences. Later (J., 1937, 387) it was suggested that the *l-* and the synthetic lactone represented the *trans-* and the *cis*-form respectively of (I; $R^1 = R^2$ = veratryl).

A more detailed examination of the action of lead tetra-acetate on the synthetic racemate has confirmed the previous observation that the *cyclo*dehydro-lactones (II) and (III) are not

produced. The product has been resolved into two crystalline *diacetates*, $C_{26}H_{30}O_{10}$ and $C_{26}H_{30}O_9$, which yield the *lactones* $C_{22}H_{24}O_7$ and $C_{22}H_{26}O_8$, respectively, on hydrolysis.


(I.)


(II.)


(III.)

The structure of these compounds has not been ascertained, but it is unlikely that they represent 1-phenylnaphthalene derivatives because the lactones $C_{22}H_{24}O_7$ and $C_{22}H_{26}O_8$ both yield 3 : 4-dinitroveratrole and veratric acid on treatment with nitric acid and permanganate respectively. The formation of 3 : 4-dinitroveratrole indicates the presence of an oxygenated veratrole group, but the yields were insufficient to establish the presence of two such groups. In view of the irregular behaviour observed with lead tetra-acetate in other cases (following paper) these observations do not rigidly exclude the suggested stereochemical relationship between the *l*- and the synthetic lactone.

A crystallographic comparison, made by Miss D. M. Crowfoot, shows that there is no direct relationship between the crystal structures of the *l*- and the synthetic lactone and this may be attributed either to structural or to stereochemical differences between the two compounds. It is not possible to decide from the crystal structures whether the lactones belong to the *cis*- or the *trans*-series. Details of the crystallographic examination will be published in a later communication.

The rates of hydrolysis of the *l*- and the synthetic lactone are indistinguishable, but the hydroxy-acid obtained from the *l*-lactone is lactonised much more rapidly than the hydroxy-acid corresponding to the synthetic lactone. Similar observations have been made with *l*-hinokinin and the synthetic isomer previously (J., 1936, 725) regarded as (I; $R^1 = R^2$ = piperonyl). When *l*-matairesinol dimethyl ether (I; $R^1 = R^2$ = veratryl), $[\alpha]_D^{19°}$ $-35°$, was subjected to the prolonged action of boiling concentrated potassium hydroxide solution, boiling alcoholic sodium ethoxide solution, or dilute sodium hydroxide solution at 180°, it was converted into a mixture of hydroxy-acids, yielding a crude lactone, $[\alpha]_D^{17°}$ $+18°$. This crude lactone was resolved by repeated crystallisation into *l*-matairesinol dimethyl ether and d-iso*matairesinol dimethyl ether*, $[\alpha]_D^{18°}$ $+78°$, from which crystalline *dinitro*- and *dibromo*-derivatives have been prepared. This *d-iso*-lactone is probably formed by inversion of the asymmetric carbon atom in the $\alpha$-position with respect to the carbonyl group, and if the *l*- and the synthetic lactone differ only in sterochemical configuration the synthetic lactone must be *dl-iso*matairesinol dimethyl ether. After the *d-iso*-lactone had been heated at 180° with dilute sodium hydroxide solution, the equilibrium mixture of lactones with $[\alpha]_D^{17°}$ $+18°$ was regenerated, but when the *d-iso*-lactone was treated with cold methyl-alcoholic potassium hydroxide, complete inversion to *l*-matairesinol dimethyl ether occurred. It is well known that Walden inversions at $\alpha$-asymmetric centres usually occur more rapidly with esters than with the anions of the corresponding carboxylic acids. The above results are explicable on the assumption that complete inversion of the *d-iso*-lactone with cold alkali is due to a Walden inversion of the $\alpha$-asymmetric centre of the lactone, and the equilibration of the *d-iso*-lactone under the more drastic alkaline conditions follows its complete inversion to the *l*-lactone in accordance with the following sequence of changes :

*d-iso*-Lactone $\xrightarrow{\text{dil. NaOH}}$ *l*-lactone $\underset{\text{HCl}}{\overset{\text{NaOH}}{\rightleftharpoons}}$ *l*-hydroxy-acid $\xleftrightarrow{\text{hot NaOH}}$ *d-iso*-hydroxy-acid

(*d-iso*-hydroxy-acid $\xrightarrow{\text{HCl}}$ *d-iso*-Lactone)

The rates of hydrolysis of the *d-iso*-lactone and the *l*-lactone were identical in accordance with the above hypothesis but, as the *d-iso*-lactone was converted into the hydroxy-acid

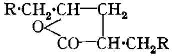
corresponding to the *l*-lactone, special conditions were necessary in order to determine the rate of lactonisation of the *d*-*iso*-hydroxy-acid. When the mixture of *d*-*iso*- and *l*-hydroxy-acids, obtained by addition of acetic acid to the equilibrium mixture of the sodium salts, was refluxed with alcohol, the *l*-acid was preferentially lactonised and the d-iso-*hydroxy-acid*, $[\alpha]_D$ $-23°$, could be isolated; its rate of lactonisation proved to be much slower than that of the *l*-acid and agreed more closely with the rate observed with the hydroxy-acid obtained from the synthetic lactone. As *d*-*iso*matairesinol dimethyl ether yielded the *cyclo*dehydro-lactones (II) and (III) on treatment with lead tetra-acetate, the failure to obtain these products from the synthetic lactone can no longer be explained by differences in stereo-chemical configuration. Furthermore, the synthetic racemate, m. p. 107°, unlike *d*-*iso*-matairesinol dimethyl ether, was stable to mild alkaline treatment. Drastic alkaline conditions converted it partly into an isomeric form; the m. p. of the recovered lactone was 97—99°, but fractional crystallisation yielded the synthetic racemate, m. p. 107°, and attempts to isolate the isomer from the mother-liquors have been unsuccessful. The crude lactone was indistinguishable from the original synthetic racemate in behaviour towards lead tetra-acetate, rate of hydrolysis, and rate of lactonisation of the derived hydroxy-acid. No conventional stereochemical explanation can be offered for the observed differences and it is now concluded that the synthetic racemate and *l*-matairesinol dimethyl ether differ structurally.

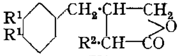
After the above experiments were completed Omaki (*J. Pharm. Soc. Japan*, 1937, **57**, 89) described the preparation of *d*-*iso*matairesinol dimethyl ether, $[\alpha]_D$ $+145°$, by methylating *d*-*iso*arctigenin, obtained by the action of alkali on *l*-arctigenin (I; $R^1$ = veratryl, $R^2$ = vanillyl). The high rotation value suggested that our specimen of *d*-*iso*matairesinol dimethyl ether might be impure, but repeated crystallisation failed to alter the $\alpha_D$ value and we are unable to account for the discrepancy. Omaki also found that the hydroxy-acid obtained from the *l*-lactone is lactonised by boiling methyl alcohol more rapidly than the *d*-*iso*-hydroxy-acid, and concludes that the *d*-*iso*- and the *l*-lactone are *trans*- and *cis*-forms respectively. The reasons for this conclusion are not apparent and our conclusions, made from essentially the same observations, are the reverse. Inspection of the formulæ or models shows that a maximum repulsion of like groups results in a greater separation of the hydroxymethyl and carboxyl groups in the case of the hydroxy-acid derived from the *cis*-lactone. Consequently it may be argued that the hydroxy-acid which lactonises the more readily will have the *trans*-configuration and it is therefore concluded that the *d*-*iso*- and the *l*-lactone are *cis*- and *trans*-forms respectively. This conclusion is consistent with that arrived at previously (J., 1937, 387) on biogenetic grounds.

One of the methods, namely, that based upon the condensation of *O*-methyleugenol oxide with methyl sodio-3 : 4-dimethoxybenzyl-α-cyanoacetate, used previously (*loc. cit.*) for the preparation of the synthetic lactone, is ambiguous; lactones (I; $R^1 = R^2$ = veratryl) or (IV; R = veratryl) could arise by reaction of the cyanoacetate anion with the β- or the γ-carbon atom respectively of the oxide chain. The synthetic lactone was also obtained, in small yield, by the action of 3 : 4-dimethoxybenzyl chloride on the lactonic condensation product of ethyl acetoacetate with *O*-methyleugenol oxide. This second method has now been improved considerably from the preparative point of view, and more convincing evidence has been obtained of the identity of the product obtained by the two methods. In addition the second method of synthesis has been applied to the methyl-enedioxy-analogue and a lactone, identical with the lactone previously regarded as *dl*-cubebinolide (J., 1936, 725), has been obtained. It follows, therefore, that the anions of ethyl acetoacetate and substituted benzylcyanoacetates unite with the same atom of the oxide chain in compounds of the *O*-methyleugenol oxide type.

Formula (V; $R^1$ = OMe, $R^2$ = $CO{\cdot}CH_3$) was preferred to (VI) for the condensation product of ethyl acetoacetate with *O*-methyleugenol oxide because it gave a simple interpretation of the formation of naphthalene derivatives (see p. 801), and important results have been obtained from a further examination of this condensation product. Hydrolysis with concentrated sodium hydroxide solution resulted in deacetylation with the formation of a crystalline lactone, $C_{13}H_{16}O_4$, which was also prepared from *O*-methyl-

eugenol oxide and ethyl malonate, and (V; $R^1 = OMe$, $R^2 = H$), (VI; $R^1 = OMe$, $R^2 = H$) and (VII) were considered as possible structures for the lactone $C_{13}H_{16}O_4$.


(IV.)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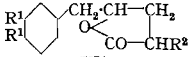
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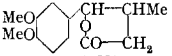
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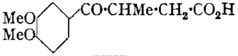
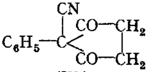
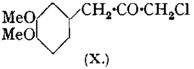
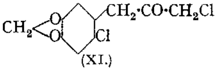
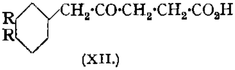

(VIII).


(IX.)

Structure (VII) was excluded by an independent synthesis; β-veratroyl-*n*-butyric acid (VIII) was reduced to the corresponding hydroxy-acid, which yielded *γ-veratryl-β-methylbutyrolactone* (VII) on lactonisation. An unambiguous synthesis of (V; $R^1 = OMe$, $R^2 = H$) has not yet been realised, but some experiments in this direction are described in the experimental section. Numerous failures were encountered in attempts to prepare (VI; $R^1 = OMe$, $R^2 = H$). Preliminary attempts to prepare γ-keto-δ-phenylvaleric acid by the action of ethyl succinate on phenylacetonitrile yielded an oil which gave *2-cyano-2-phenyl*cyclo*pentane-1 : 3-dione* (IX) on distillation, but difficulties experienced in the hydrolysis of this nitrile led to the abandonment of the method. *γ-Chloro-α-veratrylacetone* (X) has been prepared by the action of diazomethane on veratrylacetyl chloride and subsequent treatment with dry hydrogen chloride, but smooth condensation of (X) with malonic, cyanoacetic, or acetoacetic ester was not effected. No obvious explanation can be offered for these failures and an attempt to prepare the methylenedioxy-analogue of (X) under precisely the same conditions yielded a *dichloro*-compound, $C_{10}H_8O_3Cl_2$. One of the chlorine atoms was hydrolysed with alcoholic potassium hydroxide and it is possible that the dichloro-compound has structure (XI) and that it arises by dismutation in the presence of hydrogen chloride (see Krohnke, *Ber.*, 1936, **69**, 921). Eventually *γ-keto-δ-veratrylvaleric* acid (XII; R = OMe) was prepared by an application of Mrs. G. M. Robinson's method (J., 1930, 745); veratrylacetyl chloride was condensed with ethyl sodioacetosuccinate in ethereal solution and hydrolysis of the neutral product gave a small yield of the acid (XII; R = OMe). This keto-acid was reduced by means of sodium and alcohol to the corresponding hydroxy-acid, which was lactonised to *γ-(3 : 4-dimethoxybenzyl)butyrolactone* (VI; $R^1 = OMe$, $R^2 = H$), identical in all respects with the lactone obtained by deacetylating the condensation product of ethyl acetoacetate and *O*-methyleugenol oxide. The corresponding methylenedioxy-lactone (VI; $R^1R^1 = CH_2O_2$, $R^2 =$


(X.)


(XI.)

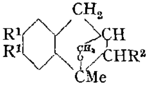

(XII.)

H), obtained similarly from piperonylacetyl chloride, was prepared from piperic acid by Fittig and Weinstein (*Annalen*, 1885, **227**, 38, 47), who describe it as an oil, yielding a crystalline hydroxy-acid, m. p. 95°. Our product is an oil, yielding the hydroxy-acid, m. p. 95°, and a crystalline *nitro*-derivative, and with the aid of these derivatives the identity of this lactone with the lactone obtained previously by deacetylating the condensation product of ethyl acetoacetate and safrole oxide (J., 1936, 351) has been established.

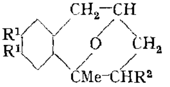
These important observations prove that the anions of ethyl acetoacetate, malonate, or substituted benzylcyanoacetates react with the γ-carbon atom of *O*-methyleugenol and safrole oxide, giving γ-substituted butyrolactones of type (VI; $R^2 = CO{\cdot}CH_3$, $CO_2Et$, or $C_6H_5{\cdot}CH_2$) and not β-substituted butyrolactones of type (V) as previously suggested. Consequently the products formerly regarded as *dl*-matairesinol dimethyl ether (I; $R^1 = R^2 =$ veratryl) and *dl*-cubebinolide (*dl*-hinokinin) (I; $R^1 = R^2 =$ piperonyl) must possess the formulæ (IV; R = veratryl) and (IV; R = piperonyl) respectively, and the differences in behaviour of the natural and the synthetic lactone towards lead tetra-acetate, hydrolytic and lactonising agents are readily understandable.

As mentioned earlier in this communication, the numerous conversions of the condens-

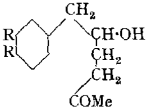
ation product of ethyl acetoacetate with safrole or *O*-methyleugenol oxide into naphthalene derivatives constituted a powerful argument for the earlier selection of structure (V; $R^2 = CO{\cdot}CH_3$) in preference to (VI; $R^2 = CO{\cdot}CH_3$). A critical review of our previous results (J., 1935, 636; 1936, 348, 725, 998; 1937, 1646; see also following paper) and further observations made during the course of the present work have strengthened the evidence that the naphthalene structure assigned to these products is correct. When α-acetyl-γ-3 : 4-dimethoxybenzylbutyrolactone (VI; $R^1 = OMe$, $R^2 = CO{\cdot}CH_3$) was treated with methyl-alcoholic hydrogen chloride, it was converted into *methyl* 6 : 7-*dimethoxy*-3 : 1-endo*methyleneoxy*-1-*methyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*-2-*carboxylate* (XIII; $R^1 = OMe$, $R^2 = CO_2Me$), and the corresponding *acid* (XIII; $R^1 = OMe$, $R^2 = CO_2H$) was prepared either by alkaline hydrolysis of the methyl ester, or directly from (VI; $R^1 = OMe$, $R^2 = CO{\cdot}CH_3$) by the action of a mixture of acetic and hydrochloric acids. The acid (XIII; $R^1 = OMe$, $R^2 = CO_2H$) was converted into 6 : 7-*dimethoxy*-1 : 3-*dimethylnaphthalene* (XVI) by heating with selenium at 280°, and the *endo*methyleneoxy-structures, or alternatives based upon the oxide structure (XIV), are necessary to explain the Zerewitinoff determinations, which proved the presence of one active hydrogen atom in the acid (XIII; $R^1 = OMe$, $R^2 = CO_2H$) and the absence of active hydrogen atoms in the methyl ester (XIII; $R^1 = OMe$, $R^2 = CO_2Me$). The lactone



(XIII.)

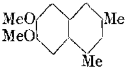


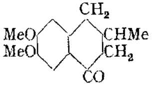
(XIV.)



(XV.)

(XVI.)

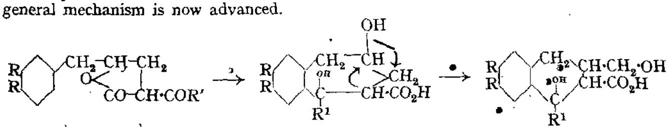




(XVII.)

(VI; $R^1 = OMe$, $R^2 = CO{\cdot}CH_3$) was hydrolysed by dilute sodium hydroxide solution to give *methyl* γ-*hydroxy*-δ-*veratrylbutyl ketone* (XV; R = OMe). This oily ketone was converted by a mixture of acetic and hydrochloric acids into 6 : 7-*dimethoxy*-3 : 1-endo-*methyleneoxy*-1-*methyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene* (XIII; $R^1 = OMe$, $R^2 = H$), which contained no active hydrogen atom and yielded 6 : 7-dimethoxy-1 : 3-dimethylnaphthalene (XVI) on dehydrogenation with selenium. The structure of the dehydrogenation product (XVI) was proved by a synthesis from β-veratroyl-*n*-butyric acid (VIII). The crude Clemmensen reduction product of (VIII) was cyclised to 1-*keto*-6 : 7-*dimethoxy*-3-*methyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene* (XVII), which was converted into (XVI) by condensation with methylmagnesium iodide and subsequent dehydrogenation with selenium. The methylenedioxy-derivatives (VI; $R^1R^1 = CH_2O_2$, $R^2 = CO{\cdot}CH_3$) and (XV; $RR = CH_2O_2$), described in Part IV (J., 1936, 351), have been converted similarly into the endo*methyleneoxy*-derivatives (XIII; $R^1R^1 = CH_2O_2$, $R^2 = CO_2H$), (XIII; $R^1R^1 = CH_2O_2$, $R^2 = CO_2Me$) and (XIII; $R^1R^1 = CH_2O_2$, $R^2 = H$), but the dehydrogenation of these compounds has not been examined.

Reference to other communications of this series shows that the formation of naphthalene derivatives does not demand the application of the selenium dehydrogenation reaction, but all cases of naphthalene formation, observed in this and previous work, involve the use of acidic cyclising agents. This suggested that the conversion of compounds of type (VI) into naphthalene derivatives involves a pinacolinic transformation and the following general mechanism is now advanced.



The scheme is applicable to lactones where $R^1$ may be a methyl or a substituted phenyl group, and the conversion of *keto-alcohols* of *type* (*XV*) into naphthalenes may be formulated in a similar manner. It is noteworthy that the formation of naphthalene derivatives has not been observed with the lactone (VI ; $R^1$ = OMe, $R^2$ = H) ; here $R^1$·CO is replaced by H, and as the synthetic lactone (IV ; R = veratryl) differs structurally from, and is not converted by acidic reagents into either *iso*- or matairesinol dimethyl ether, it is probable that the pinacolinic change is dependent upon a cyclisation reaction. The above scheme represents a typical pinacolinic transformation and there is evidence from the chemistry of the azulenes (Pfau and Plattner, *Helv. Chim. Acta*, 1936, **19**, 858) that the *cyclo*pentane*cyclo*heptane ring system is capable of rearrangement to naphthalene compounds.

All experimental observations in this and in other papers of this series are in complete harmony with this modified interpretation of the reactions. The structures formerly assigned to the naphthalene derivatives remain undisturbed, and previous conclusions with regard to the structure of natural products of the lignan family are not invalidated. It is necessary to modify the structures of the butyrolactones which were previously regarded as substituted β-benzylbutyrolactones of type (V), to the corresponding substituted γ-benzylbutyrolactone structure (VI). In the same way keto-alcohols previously formulated as primary alcohols of the methyl (or phenyl) β-hydroxymethyl-γ-phenylpropyl ketone type must be altered to the secondary alcoholic, methyl (or phenyl) γ-hydroxy-δ-phenylbutyl ketone structure (as XV). A list of corrected structures is appended together with references to the erroneous formulations.

γ-(3 : 4-Methylenedioxybenzyl)butyrolactone, J., 1936, 349, 351 (V; R = H).

α-Acetyl-γ-(3 : 4-methylenedioxybenzyl)butyrolactone, *ibid.* (V; R = CO·$CH_3$).

Ethyl γ-(3 : 4-methylenedioxybenzyl)butyrolactone-α-carboxylate, *ibid.* (V; R = $CO_2$Et).

α-Acetyl-α-(3 : 4 : 5-trimethoxybenzoyl)-γ-(3 : 4-methylenedioxybenzyl)butyrolactone, *ibid.* (VII; R = CO·$CH_3$).

Ethyl α-acetyl-α-(3 : 4 : 5-trimethoxybenzoyl)-γ-(3 : 4-methylenedioxybenzyl)butyrolactone-α-carboxylate, *ibid.* (VII; R = $CO_2$H).

α-(3 : 4 : 5-Trimethoxybenzoyl)-γ-(3 : 4-methylenedioxybenzyl)butyrolactone, *ibid.* (VII; R = H).

Methyl γ-hydroxy-δ-piperonylbutyl ketone, *ibid.* (VIII).

α-Acetyl-γ-(3 : 4-dimethoxybenzyl)butyrolactone, J., 1936, 725, 727 (IV).

α-Veratroyl-γ-(3 : 4-dimethoxybenzyl)butyrolactone, *ibid.* (V) and J., 1937, 1646, 1648.

α-Piperonyl-γ-(3 : 4-methylenedioxybenzyl)butyrolactone, J., 1936, 727.

α-Acetyl-αγ-bis-(3 : 4-dimethoxybenzyl)butyrolactone, *ibid.*, pp. 725, 728 (VIII).

αγ-Bis-(3 : 4-dimethoxybenzyl)butyrolactone, *ibid.* (III; R = OMe).

αγ-Bis-(3 : 4-methylenedioxybenzyl)butyrolactone, *ibid.*, pp. 727, 729 (III; RR = $CH_2O_2$).

α-Acetyl-γ-(3-methoxy-4-ethoxybenzyl)butyrolactone, J., 1936, 999, 1001.

α-Veratroyl-γ-(3-methoxy-4-ethoxybenzyl)butyrolactone, *ibid.*, p. 1001.

α-(3-Methoxy-4-ethoxybenzoyl)-γ-(3 : 4-dimethoxybenzyl)butyrolactone, *ibid.*, p. 1001

α-(3-Methoxy-4-ethoxybenzyl)-γ-(3 : 4-dimethoxybenzyl)butyrolactone, *ibid.*, pp. 999, 1001 (I).

α-(3 : 4-Dimethoxybenzyl)-γ-(3-methoxy-4-ethoxybenzyl)butyrolactone, *ibid.* (II).

Veratryl γ-hydroxy-δ-veratrylbutyl ketone, J., 1937, 1646, 1648 (IX).

## EXPERIMENTAL.

*αγ-Bis-(3 : 4-methylenedioxybenzyl)butyrolactone* (IV; R = piperonyl).—*α-Acetyl-αγ-bis-(3 : 4-methylenedioxybenzyl)butyrolactone* (4·1 g.) was prepared from 3 : 4-methylenedioxybenzyl chloride (3·5 g.) and the sodio-derivative of α-acetyl-γ-(3 : 4-methylenedioxybenzyl)butyrolactone (4 g.) (VI; $R^1R^1$ = $CH_2O_2$, $R^2$ = CO·$CH_3$) exactly as described (J., 1936, 728) in the case of the corresponding 3 : 4-dimethoxybenzyl derivative. The product was an

alkali-insoluble oil, b. p. 270—280°/1 mm., giving no colour with ferric chloride (Found : C, 66·8; H, 5·1. $C_{22}H_{20}O_7$ requires C, 66·7; H, 5·0%). The lactone (1 g.) was refluxed for 1 hour with alcohol (10 c.c.) and 5% sodium hydroxide solution (10 c.c.), water added, and neutral matter removed in chloroform. The alkaline liquor was acidified, lactonised by boiling for 5 minutes, and extracted with chloroform. The extract was washed with sodium bicarbonate solution and dried, and the solvent removed. The product (IV; R = piperonyl) crystallised from methyl alcohol in colourless prisms (0·4 g.), m. p. 107—108° (Found : C, 67·8; H, 5·1. Calc. for $C_{20}H_{18}O_6$ : C, 67·8; H, 5·1%), which gave no depression in m. p. when mixed with the compound obtained previously (J., 1936, 729) from safrole oxide and methyl 3 : 4-methylenedioxybenzyl-α-cyanoacetate. Identity was confirmed by comparison of the dibromo- and dinitro-derivatives, m. p.'s 123° and 161° respectively.

*αγ-Bis-*(3 : 4-*dimethoxybenzyl*)*butyrolactone* (IV; R = veratryl).—α-Acetyl-αγ-bis-(3 : 4-dimethoxybenzyl)butyrolactone (1·8 g.) (J., 1936, 728) was hydrolysed with aqueous alcoholic sodium hydroxide as described above; the lactone (IV; R = veratryl) (0·7 g.), m. p. 106—107° (Found : C, 68·4; H, 6·9. Calc. for $C_{22}H_{26}O_6$ : C, 68·4; H, 6·7%), obtained was identical with the product described previously (J., 1936, 728) and identity was confirmed by the preparation of the dibromo- and dinitro-derivatives, m. p.'s 110° and 179° respectively.

*Action of Oxidising Agents on Matairesinol Dimethyl Ether* (I; $R^1 = R^2$ = veratryl) *and the Synthetic Lactone* (IV; R = veratryl).—(a) *Potassium permanganate.* The synthetic lactone (IV; R = veratryl) was oxidised with potassium permanganate as described previously (J., 1935, 635) for matairesinol dimethyl ether. Veratric acid, m. p. 179—180°, was obtained in similar yield.

(b) *Sodium hypobromite.* The synthetic lactone, or matairesinol dimethyl ether (0·3 g.), was dissolved in 1% methyl-alcoholic potassium hydroxide (10 c.c.), refluxed for 10 minutes, the alcohol removed, and the hydroxy-acid salt dissolved in water (10 c.c.). A solution of bromine (0·5 c.c.) in 10% sodium hydroxide solution (12 c.c.) was added and, after refluxing for 3 hours, the solution was treated with sulphur dioxide, acidified with dilute sulphuric acid, and extracted with chloroform. The acids were removed from the extract by washing with sodium bicarbonate solution and recovered; crystallisation from hot water gave veratric acid (0·26 g.), m. p. 180°. Reduction of the amount of sodium hypobromite led to recovery of lactone and a diminution in yield of veratric acid.

(c) *Lead tetra-acetate.* The action of lead tetra-acetate on *l*-matairesinol dimethyl ether has been described (J., 1935, 635). The synthetic lactone (IV; R = veratryl) (0·5 g.) in acetic acid (5 c.c.) was treated at 70° with lead tetra-acetate (1·2 g.) in acetic acid (15 c.c.) for 20 minutes. Water was added, the product extracted with chloroform, the extract washed with sodium bicarbonate solution and dried, and the solvent removed. The residue solidified on trituration with a little methyl alcohol; the solid (0·4 g.), m. p. 140—150°, was collected and resolved by fractional crystallisation from benzene into two *diacetates*, A and B. The sparingly soluble compound, A, separated from benzene in colourless slender needles, m. p. 150—151° (Found : C, 64·4, 64·5; H, 6·1, 6·4; $CH_3$·CO, 16·7, 17·7. $C_{26}H_{30}O_9$ requires C, 64·2; H, 6·2; 2$CH_3$·CO, 17·7%). B crystallised from benzene–ether in colourless prisms, m. p. 158—159° (Found : C, 62·4, 62·5; H, 5·9, 6·0; $CH_3$·CO, 17·7, 18·0. $C_{26}H_{30}O_{10}$ requires C, 62·2; H, 6·0; 2$CH_3$·CO, 17·1%). The substance A (0·1 g.) was hydrolysed with 2% methyl-alcoholic sodium hydroxide (10 c.c.) on the water-bath for 10 minutes. The alcohol was removed, water (10 c.c.) added, and the solution acidified and heated on the water-bath for ½ hour; the product, C, isolated with chloroform, separated from methyl alcohol in slender prisms, m. p. 101—103° (Found : C, 63·2, 63·4; H, 6·2, 6·4. $C_{22}H_{26}O_8$ requires C, 63·2; H, 6·3%). In the same way, hydrolysis of B gave D, which crystallised from methyl alcohol in slender prisms, m. p. 147—148° (Found : C, 66·1, 66·3; H, 6·1, 6·2. $C_{22}H_{24}O_7$ requires C, 66·0; H, 6·0%). The compounds C and D contained no acetyl groups, gave no colour with tetranitromethane, and on oxidation with potassium permanganate in faintly alkaline solution they (0·2 g.) yielded veratric acid (0·05 g.). C or D (0·1 g.) was boiled with concentrated nitric acid (1 c.c.) for 5 minutes, and water added; the neutral product, isolated with ether, crystallised from methyl alcohol in pale yellow needles (0·02 g.), m. p. 126—127°, not depressed by 4 : 5-dinitroveratrole. The new formula (IV; R = veratryl) for the synthetic lactone does not simplify the interpretation of the structures of A, B, C, and D.

d-iso*Matairesinol Dimethyl Ether* (I; $R^1 = R^2$ = veratryl). (a) *l*-Matairesinol dimethyl ether (5 g.), $[\alpha]_D^{19°}$ −36°, was warmed for 5 minutes with a solution of sodium methoxide (from 0·64 g. of sodium) in methyl alcohol (25 c.c.), and the solution evaporated to dryness under reduced pressure. The sodium salt of the hydroxy-acid was dissolved in water (40 c.c.) and

heated in a sealed tube at 180° for 24 hours. The solution was acidified with dilute hydrochloric acid, lactonised by boiling for 5 minutes, and extracted with chloroform, and the extract washed with 1% sodium hydroxide solution. Removal of the solvent yielded a crude lactone (4·5 g.), m. p. 102—109°, $[\alpha]_D^{17°}$ +18·7° in chloroform (*c* = 7·91).

(*b*) *l*-Matairesinol dimethyl ether (5 g.), boiled with 50% potassium hydroxide solution (25 c.c.) for 24 hours, afforded a crude lactone (4·0 g.), $[\alpha]_D^{17°}$ +18·4° in chloroform (*c* = 9·24).

(*c*) *l*-Matairesinol dimethyl ether (5 g.), refluxed with a solution of sodium (2 g.) in absolute alcohol (20 c.c.) in a nitrogen atmosphere for 5 days, gave a crude lactone (3·5 g.), $[\alpha]_D^{17°}$ +17·9° in chloroform (*c* = 5·25).

Fractional crystallisation from methyl alcohol resolved the crude lactone (4·5 g.) into head and tail fractions, from which pure *l*-matairesinol dimethyl ether (2·1 g.) and d-iso*matairesinol dimethyl ether* (1·7 g.) respectively were isolated. During the separation frequent use was made of the greater speed of solution of the *d-iso*-form in methyl alcohol. *d-iso*Matairesinol dimethyl ether separated from methyl alcohol in long, feathery needles, m. p. 111—112°, $[\alpha]_D^{19°}$ +78° in chloroform (*c* = 4·01), and this value was unchanged after further crystallisations (Found: C, 68·4; H, 6·8. $C_{22}H_{26}O_6$ requires C, 68·4; H, 6·7%). Attempts to convert *d-iso*matairesinol dimethyl ether into the corresponding hydroxy-acid by the action of cold methyl-alcoholic potassium or barium hydroxide resulted in a quantitative recovery of *l*-matairesinol dimethyl ether. When heated with dilute sodium hydroxide solution at 180° for 24 honrs, the *d-iso*-lactone was converted into the equilibrium mixture with $[\alpha]_D^{17°}$ +18°. *d-iso*Matairesinol dimethyl ether was converted into the *cyclo*dehydro-lactones (II) and (III) by the action of lead tetra-acetate as described previously (J., 1935, 633) for the *l*-lactone.

*Dibromo*-d-iso*matairesinol dimethyl ether*, prepared in acetic acid solution, separated from alcohol in long needles, m. p. 144°, $[\alpha]_D^{20°}$ +18·8° (*c* = 1·15) in chloroform (Found: C, 48·2; H, 4·2. $C_{22}H_{24}O_6Br_2$ requires C, 48·5; H, 4·5%). *Dinitro*-d-iso*matairesinol dimethyl ether*, prepared in acetic acid solution, separated from alcohol–chloroform in pale yellow plates, m. p. 161—162°, $[\alpha]_D^{20°}$ +105·5° in chloroform (*c* = 1·20) (Found after drying at 100°: C, 55·4; H, 5·2. $C_{22}H_{24}O_{10}N_2$ requires C, 55·4; H, 5·0%). The crystals probably contain solvent of crystallisation which is lost at 100° with modification of the crystalline form.

*Rates of Hydrolysis of Lactones.*—Excess of N/20-barinm hydroxide was added to N/100-methyl-alcoholic solutions of the lactones and the rates of hydrolysis at 15° were determined by titrating aliquot portions with N/20-hydrochloric acid at snitable intervals. No special accuracy was aimed at, but the figures in Table I were reproducible to within 5% of the values given.

TABLE I.

| | Time in hours: | 0·5. | 1·5. | 3. | 6. | 8. | 12. | 17. |
|---|---|---|---|---|---|---|---|---|
| % Hydrolysis at 15°. | *l*-Matairesinol dimethyl ether | 21 | 42 | 58 | 76 | 85 | 94 | 97 |
| | *d-iso*Matairesinol dimethyl ether | 21 | 40 | 56 | 76 | 84 | 94 | — |
| | αγ-Bis-(3 : 4-dimethoxybenzyl)-butyrolactone | 23 | 41 | 60 | 78 | 86 | — | — |
| | *l*-Hinokinin | 17 | 34 | 58 | 80 | 88 | — | — |
| | αγ-Bis-(3 : 4-methylenedioxybenzyl)-butyrolactone | 17 | 35 | 57 | 79 | 87 | — | — |

l-*Matairesinolic Acid Dimethyl Ether.*—*l*-Matairesinol dimethyl ether (1 g.) was warmed for 5 minutes with sodium methoxide (from 0·08 g. of sodium) in methyl alcohol (10 c.c.). The alcohol was removed, the sodium salt dissolved in water (15 c.c.), and the well-cooled solution carefully acidified with dilute acetic acid. The precipitate was collected, washed with water, and dissolved in a little cold acetone, and water gradually added; the *hydroxy-acid* separated in long prisms, which melted at 90—95° with loss of water, resolidified, and melted again at 127° (Found after drying over phosphoric oxide: C, 65·5; H, 7·0. $C_{22}H_{28}O_7$ requires C, 65·3; H, 6·9%). $[\alpha]_D^{18°}$ −32° in alcohol (*c* = 1·00).

*γ-Hydroxy-αγ-bis-*(3 : 4-*dimethoxybenzyl*)*butyric acid*, obtained similarly from the synthetic lactone (IV; R = veratryl) and isolated with chloroform, was an oil (Found after drying in a desiccator: C, 65·1; H, 7·1. $C_{22}H_{28}O_7$ requires C, 65·3; H, 6·9%).

d-iso*Matairesinolic Acid Dimethyl Ether.*—*l*-Matairesinol dimethyl ether was heated in a sealed tube with sodium hydroxide solution at 180° as described on p. 803. The mixed hydroxy-acids, precipitated with acetic acid, were dried in a desiccator, dissolved in alcohol, and boiled for 2 hours. The alcohol was removed, sodium bicarbonate solution added, and lactonic matter removed with chloroform. Addition of acetic acid to the bicarbonate liquor precipitated a gum, which slowly solidified and crystallised from aqueous alcohol in

small prisms, m. p. 160° (Found: C, 65·4; H, 6·8. $C_{22}H_{26}O_7$ requires C, 65·3; H, 6·9%). $[\alpha]_D^{15°}$ −23° in alcohol ($c$ = 1·03). Lactonisation with hot dilute mineral acid yielded *d-iso*-matairesinol dimethyl ether, m. p. 111°. $[\alpha]_D^{19°}$ +78°.

*Rates of Lactonisation of Hydroxy-acids.*—Two methods were employed: (a) Excess of N/20-barium hydroxide was added to N/100-methyl-alcoholic solutions of the lactones. After 24 hours at 15° the concentration of the hydroxy-acid was determined by neutralisation with N/20-hydrochloric acid. An additional quantity of N/20-hydrochloric acid was then added to liberate the hydroxy-acid from its barium salt; a slight deficiency was used to prevent catalysis by free mineral acid. The solution was heated at 59° under reflux, and aliquot portions titrated at intervals with N/20-barium hydroxide (Table II). (b) As method (a) was not applicable for the *d-iso*-hydroxy-acid, the following was adopted. An N/100-solution of the hydroxy-acid in alcohol (250 c.c.) was diluted to 350 c.c. with water and heated at 59°. Aliquot portions were titrated at intervals with N/20-barium hydroxide (Table III). Results (*) in Table III illustrate the catalytic influence of mineral acids; the measurements were made with N/100-methyl-alcoholic solutions of the hydroxy-acids (250 c.c.), made up to 350 c.c. with N/40-hydrochloric acid. The figures in Tables II and III were reproducible to within 4% of the values recorded.

TABLE II.

| | Time in hours: | 1. | 2. | 4. | 6. | 10. | 20. |
|---|---|---|---|---|---|---|---|
| % Lactonisation at 59°. | *l*-Matairesinol dimethyl ether or *d-iso*matairesinol dimethyl ether | 11 | 17 | 25 | 31 | 44 | 74 |
| | αγ-Bis-(3 : 4-dimethoxybenzyl)-butyrolactone; either before or after action of alkali at 180° | 8·5 | 11 | 12 | 14 | 19 | 24 |
| | *l*-Hinokinin | 19 | 27 | 37 | 43 | 53 | — |
| | αγ-Bis-(3 : 4-methylenedioxybenzyl)-butyrolactone | 13 | 15 | 18 | — | 24 | 29 |

TABLE III.

| | Time in hours: | 1. | 2. | 4. | 6. | 10. | 20. |
|---|---|---|---|---|---|---|---|
| % Lactonisation at 59°. | *l*-Matairesinolic acid dimethyl ether | 6 | 11 | 19 | 24 | 31 | 42 |
| | | * 95·5 | 97 | 98 | — | — | — |
| | *d-iso*Matairesinolic acid dimethyl ether | 3 | 4 | 5 | 6 | 7 | 9 |
| | | * 35 | 54 | 75 | 87 | — | — |
| | γ-Hydroxy-αγ-bis-(3 : 4-dimethoxybenzyl)butyric acid | 4 | 6 | 8·5 | 10 | 12 | 13 |

*γ-Veratryl-β-methylbutyrolactone* (VII).—β-Veratroyl-*n*-butyric acid (VIII) (1 g.) (this vol., p. 811) in absolute alcohol (25 c.c.) was gradually added to molten sodium (4 g.) in an oil-bath at 160°. After heating for 1 hour at 160—180°, the solution was cooled and diluted with water, the alcohol removed, and the mixture acidified and lactonised by boiling for 15 minutes. The product was extracted with chloroform, the extract washed with sodium bicarbonate solution, and the chloroform removed; the residue crystallised from ether–light petroleum in colourless prisms, m. p. 112—113° (Found: C, 66·3; H, 7·1. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%).

*2-Cyano-2-phenyl*cyclo*pentane-1 : 3-dione* (IX).—Phenylacetonitrile (5·8 g.), ethyl succinate (8·7 g.), and sodium ethoxide (from 1·15 g. of sodium) in alcohol (25 c.c.) were refluxed for 4 hours. After addition of water and removal of neutral matter with ether, the alkaline solution was acidified. The product, isolated with ether, was an oil, which on distillation at 1 mm. yielded a fraction (3 g.), b. p. about 120°, and a fraction (4·5 g.), b. p. 180—190°/1 mm. The latter solidified and crystallised from methyl alcohol–chloroform in long flat prisms, m. p. 149° (Found: C, 72·5; H, 4·5. $C_{12}H_9O_2N$ requires C, 72·3; H, 4·6%). The compound contained nitrogen and gave no coloration with ferric chloride.

*γ-Chloro-α-veratrylacetone* (X).—Pure veratrylacetic acid (2·5 g.) was warmed gently with pure thionyl chloride (5 g.) for 20 minutes; the excess of thionyl chloride was removed under reduced pressure, the final traces were eliminated by two additions and subsequent removals of benzene, and the residual acid chloride was dissolved in ether (10 c.c.) and gradually added with cooling to a solution of diazomethane (from 6 c.c. of nitrosomethylurethane) in ether (30 c.c.). After 3 hours, ethereal hydrogen chloride was added until evolution of nitrogen ceased, the solution was washed, first with water and then with sodium bicarbonate solution, and dried, and the solvent removed. The residual oil crystallised from ether–light petroleum in colourless needles (2·3 g.), m. p. 52° (Found: C, 57·7; H, 5·4; Cl, 15·0. $C_{11}H_{13}O_3Cl$ requires C, 57·7; H, 5·7; Cl, 15·5%), which rapidly deposited sodium chloride on addition to alcoholic sodium ethoxide.

*α-(2-Chloropiperonyl)-γ-chloroacetone* (XI).—Piperonylacetic acid (5·0 g.), treated in precisely the same way, gave a *dichloro*-compound, possibly (XI), which crystallised from ether–light petroleum in colourless needles (4 g.), m. p. 107—108° (Found: C, 48·5; H, 3·3; Cl, 28·0. $C_{10}H_8O_3Cl_2$ requires C, 48·2; H, 3·2; Cl, 28·7%). This dichloro-compound was boiled with excess of 10% methyl-alcoholic potassium hydroxide for 3 hours; the alcohol was removed, neutral matter extracted with ether, the alkaline liquor acidified with nitric acid, and the hydrolysable chlorine estimated volumetrically (Found: Cl, 14·6. $C_{10}H_8O_3Cl_2$ requires 1Cl, 14·4%).

*γ-(3 : 4-Dimethoxybenzyl)butyrolactone* (VI; $R^1$ = OMe, $R^2$ = H).—(a) α-Acetyl-γ-(3 : 4-dimethoxybenzyl)butyrolactone (VI; $R^1$ = OMe, $R^2$ = CO·$CH_3$) (1 g.) (J., 1936, 727) was heated on a water-bath for 5 hours with 20% methyl-alcoholic potassium hydroxide (10 c.c.). Water was added, the methyl alcohol removed, and neutral products containing methyl γ-hydroxy-δ-veratrylbutyl ketone (see p. 807) extracted with ether. The alkaline liquor was acidified and lactonised, and the product, isolated with ether, crystallised from ether–methyl alcohol; yield, 0·3 g.

(b) *O*-Methyleugenol oxide (3·9 g.) was added to a solution of ethyl sodiomalonate (from 0·46 g. of sodium and 3·2 g. of ethyl malonate) in alcohol (20 c.c.). After 4 days the crystalline sodio-derivative was collected, washed with a little alcohol and ether, and decomposed with dilute sulphuric acid. The product, isolated with ether, was boiled with a slight excess of 10% methyl-alcoholic potassium hydroxide for 30 minutes and after removal of the alcohol, the solution was acidified, lactonised, and extracted with chloroform. The extract was washed with sodium bicarbonate solution, the solvent removed, and the residue distilled (b. p. 190—200°/1 mm.) and crystallised; yield, 0·8 g.

(c) A solution of veratrylacetyl chloride (prepared from 10 g. of the acid as described on p. 805) in ether (50 c.c.) was added slowly with stirring to an ice-cold solution of ethyl sodioacetosuccinate (from 1·3 g. of sodium and 12 g. of the ester) in ether (50 c.c.). After 12 hours, the mixture was refluxed for 15 minutes and poured into water. The ethereal layer was rapidly washed with 1% sodium hydroxide solution and then shaken for 4 hours with 4% sodium hydroxide solution (120 c.c.). The alkaline layer was acidified and extracted with ether, the extract dried, and the solvent removed. The residual oil, which gave a red ferric test, was boiled for 12 hours with 5% sulphuric acid (80 c.c.) and the acidic products, isolated with ether, were taken up in sodium hydroxide solution and saturated with sulphur dioxide. After removal of impurities in ether, the aqueous layer was acidified, heated on the water-bath for 30 minutes, and extracted with ether. Removal of the ether yielded *γ-keto-δ-veratrylvaleric acid* (XII; R = OMe) (1·2 g.) as an oil (Found after drying in a desiccator: C, 62·1; H, 6·6. $C_{13}H_{16}O_5$ requires C, 61·9; H, 6·4%). The keto-acid (XII; R = OMe) (1 g.) was dissolved in absolute alcohol (30 c.c.) and added gradually to sodium (4 g.) at 180°. After 3 hours, the lactone was isolated as described in a similar case (p. 805) and was purified first by distillation at 1 mm. and then by crystallisation; yield, 0·6 g.

*γ-(3 : 4-Dimethoxybenzyl)butyrolactone* (VI; $R^1$ = OMe, $R^2$ = H) obtained by methods (a), (b), and (c), crystallised from ether–methyl alcohol in colourless needles, m. p. 83—84° (Found: C, 66·2; H, 7·0. $C_{13}H_{16}O_4$ requires C, 66·0; H, 6·8%). The *nitro*-derivative, prepared in acetic acid solution, separated from methyl alcohol in pale yellow prisms, m. p. 115—116° (Found: C, 55·5; H, 5·5. $C_{13}H_{15}O_6N$ requires C, 55·5; H, 5·4%). Oxidation with sodium hypobromite or potassium permanganate converted the lactone (VI; $R^1$ = OMe, $R^2$ = H) into veratric acid, and the lactone was recovered from attempted cyclisations with methyl-alcoholic hydrogen chloride, acetic–hydrochloric acid, and 80% sulphuric acid.

*γ-(3 : 4-Methylenedioxybenzyl)butyrolactone* (VI; $R^1R^1$ = $CH_2O_2$, $R^2$ = H).—This compound, obtained previously (J., 1936, 351) (a) from ethyl malonate and safrole oxide and (b) by hydrolysis of α-acetyl-γ-(3 : 4-methylenedioxybenzyl)butyrolactone (VI; $R^1R^1$ = $CH_2O_2$, $R^2$ = CO·$CH_3$), is an oil. Condensation of piperonyl chloride (10 g.) and ethyl sodioacetoglutarate, and hydrolysis of the product as described above for the dimethoxy-analogue, yielded γ-keto-δ-piperonylvaleric acid (XII; RR = $CH_2O_2$) (1·3 g.), which crystallised from ether–light petroleum in long needles, m. p. 87° (Fittig and Weinstein, *loc. cit.*, give 87°) (Found: C, 60·9; H, 5·2. Calc. for $C_{12}H_{12}O_5$: C, 61·0; H, 5·1%). Reduction of this keto-acid (1 g.) with sodium and alcohol as described above yielded the lactone (VI; $R^1R^1$ = $CH_2O_2$, $R^2$ = H) as an oil (0·8 g.), b. p. 170—180°/0·1 mm. The identity of the oil prepared by the three methods has been established by comparison of crystalline derivatives. The *nitro*-derivative, prepared in acetic acid solution, crystallised from methyl alcohol in pale yellow prisms, m. p. 98—99° (Found: C, 54·2; H, 4·3. $C_{12}H_{11}O_6N$ requires C, 54·3; H, 4·2%). The hydroxy-acid, prepared by hydrolysis with barium hydroxide, crystallised from ether–light petroleum in

colourless plates, m. p. 95° (Fittig and Weinstein, *loc. cit.*, give 95°) (Found: C, 60·8; H, 5·7. Calc. for $C_{12}H_{14}O_5$: C, 60·6; H, 5·9%).

*Methyl γ-hydroxy-δ-veratrylbutyl ketone* (XV; R = OMe) was obtained as an oil, b. p. 185—188°/0·3 mm. (Found: C, 66·4; H, 8·2. $C_{14}H_{20}O_4$ requires C, 66·7; H, 8·0%), by the action of 2% sodium hydroxide solution on α-acetyl-γ-(3 : 4-dimethoxybenzyl)butyrolactone (VI; $R^1$ = OMe, $R^2$ = CO·$CH_3$) as described previously (J., 1936, 351) for the methylenedioxy-analogue.

*6 : 7-Dimethoxy-3 : 1-*endo*methyleneoxy-1-methyl-1 : 2 : 3 : 4-tetrahydronaphthalene* (XIII; $R^1$ = OMe, $R^2$ = H).—Concentrated hydrochloric acid (9 c.c.) was added to a solution of the above keto-alcohol (XV; R = OMe) (1 g.) in glacial acetic acid (5 c.c.) and after 24 hours the mixture was diluted with water and extracted with ether; the extract was washed with sodium bicarbonate solution and dried, and the solvent removed. The residue crystallised from light petroleum in compact prisms (0·75 g.), m. p. 96° (Found: C, 71·6; H, 7·8. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%). Zerewitinoff determinations showed the absence of hydroxyl groups and the compound was recovered after heating with potassium hydrogen sulphate at 180°.

*6 : 7-Methylenedioxy-3 : 1-*endo*methyleneoxy-1-methyl-1 : 2 : 3 : 4-tetrahydronaphthalene* (XIII; $R^1R^1$ = $CH_2O_2$, $R^2$ = H), obtained similarly from methyl γ-hydroxy-δ-piperonylbutyl ketone (XV; RR = $CH_2O_2$) (J., 1936, 351) and acetic–hydrochloric acid, separated from light petroleum in colourless prisms, m. p. 85—86° (Found: C, 71·3; H, 6·4. $C_{13}H_{14}O_3$ requires C, 71·6; H, 6·5%). Hydroxyl groups were absent and the compound was not dehydrated with potassium hydrogen sulphate at 180°.

*6 : 7-Dimethoxy-3 : 1-*endo*methyleneoxy-1-methyl-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylic Acid* (XIII; $R^1$ = OMe, $R^2$ = $CO_2H$).—Concentrated hydrochloric acid (9 c.c.) was added to a solution of α-acetyl-γ-(3 : 4-dimethoxybenzyl)butyrolactone (VI; $R^1$ = OMe, $R^2$ = CO·$CH_3$) (1 g.) in glacial acetic acid (10 c.c.) and after 24 hours the mixture was diluted with water and extracted with chloroform; the extract was washed several times with water, and the solvent removed. The residue separated from ether–light petroleum in colourless stout prisms (0·7 g.), m. p. 182—183° (Found: C, 64·5; H, 6·7; OH, 10·0. $C_{15}H_{18}O_5$ requires C, 64·7; H, 6·5; OH, 9·6%). The *methyl* ester (XIII; $R^1$ = OMe, $R^2$ = $CO_2Me$), prepared in 80% yield by the action of boiling methyl-alcoholic hydrogen chloride on the lactone (VI; $R^1$ = OMe, $R^2$ = CO·$CH_3$), and isolated with chloroform, crystallised from methyl alcohol in colourless prisms, m. p. 142° (Found: C, 65·7; H, 6·9. $C_{16}H_{20}O_5$ requires C, 65·7; H, 6·9%). This ester contained no hydroxyl groups and on hydrolysis with methyl-alcoholic potassium hydroxide yielded the acid, m. p. 182—183°.

*6 : 7-Methylenedioxy-3 : 1-*endo*methyleneoxy-1-methyl-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylic acid* (XIII; $R^1R^1$ = $CH_2O_2$, $R^2$ = $CO_2H$), obtained in 70% yield from α-acetyl-γ-(3 : 4-methylenedioxybenzyl)butyrolactone (VI; $R^1R^1$ = $CH_2O_2$, $R^2$ = CO·$CH_3$) by the action of acetic–hydrochloric acid, separated from ether–light petroleum in stout prisms, m. p. 219—220° (Found: C, 64·3; H, 5·7; OH, 11·0. $C_{14}H_{14}O_5$ requires C, 64·1; H, 5·4; OH, 10·5%). The *methyl* ester (XIII; $R^1R^1$ = $CH_2O_2$, $R^2$ = $CO_2Me$), obtained in 70% yield by the action of methyl-alcoholic hydrogen chloride on the lactone (VI; $R^1R^1$ = $CH_2O_2$, $R^2$ = CO·$CH_3$), separated from methyl alcohol in prisms, m. p. 156—157° (Found: C, 65·5; H, 6·0. $C_{15}H_{16}O_5$ requires C, 65·2; H, 5·8%). Hydroxyl groups were absent and hydrolysis gave the acid, m. p. 219—220°.

*6 : 7-Dimethoxy-1 : 3-dimethylnaphthalene* (XVI).—(a) The compound (XIII; $R^1$ = OMe, $R^2$ = H) or the acid (XIII; $R^1$ = OMe, $R^2$ = $CO_2H$) (1 part) was heated with selenium (1 part) at 280° for 12 hours. A chloroform extract of the product was evaporated, the residue extracted with light petroleum (carbon), and the solvent removed. A methyl-alcoholic solution of picric acid was added to the product, and the recrystallised picrate, m. p. 116—118°, was decomposed by shaking its ethereal solution with dilute aqueous ammonia. (b) A suspension of β-veratroyl-*n*-butyric acid (VIII) (2 g.) in concentrated hydrochloric acid (15 c.c., added in two portions) was refluxed with amalgamated zinc (12 g.) for 12 hours. The oily product (2 g.), isolated with chloroform, was heated in the water-bath for 30 minutes with 80% sulphuric acid (8 c.c.), water added, and the mixture extracted with chloroform. The extract was washed with dilute sodium hydroxide solution and dried, and the solvent removed; the residual 1-*keto-6 : 7-dimethoxy-3-methyl-1 : 2 : 3 : 4-tetrahydronaphthalene* crystallised from ether–light petroleum or a small amount of methyl alcohol in large prisms (1·3 g.), m. p. 132—133° (Found: C, 70·8; H, 7·5. $C_{13}H_{16}O_3$ requires C, 70·8; H, 7·4%). A solution of methylmagnesium iodide (from 0·07 g. of magnesium and 0·4 g. of methyl iodide) in ether (5 c.c.) was added to a solution of the ketone (0·5 g.) in benzene (5 c.c.); after refluxing for 30 minutes, the mixture was decomposed with

dilute hydrochloric acid and the product (0·5 g.) was dehydrogenated with selenium (1 g.) at 280° and isolated as described above.

6 : 7-*Dimethoxy*-1 : 3-*dimethylnaphthalene* (XVI), prepared by methods (a) and (b), separated from light petroleum in rosettes of long prisms, m. p. 97—98° (Found: C, 77·7; H, 7·5. $C_{14}H_{16}O_2$ requires C, 77·7; H, 7·4%). The *picrate* crystallised from methyl alcohol in red needles, m. p. 119—120° (Found: C, 53·4; H, 4·4. $C_{14}H_{16}O_2,C_6H_3O_7N_3$ requires C, 53·8; H, 4·3%).

The following compounds were prepared during the course of this research.

*α-Cyano-β-(O-benzylvanillyl)acrylic Acid.*—A 25% aqueous solution of sodium cyanoacetate (20 c.c.) was added to a warm solution of *O*-benzylvanillin (9 g.) in alcohol (5 c.c.). 20% Sodium hydroxide solution (5 c.c.) was added, and the mixture shaken with cooling for 1 hour. The pale yellow solid which rapidly separated was decomposed with hydrochloric acid, and the *acid* was collected and crystallised from methyl alcohol; yellow needles (11 g.), m. p. 202°, were obtained (Found: C, 70·1; H, 4·7. $C_{18}H_{15}O_4N$ requires C, 69·8; H, 4·9%).

*Methyl α-cyano-β-(O-benzylvanillyl)propionate* was prepared by adding 2% sodium amalgam (300 g.) with rapid stirring and ice-cooling to a suspension of the above acid (10 g.) in water (250 c.c.). Acidification yielded a gummy acid, which was isolated with chloroform and esterified by boiling with 4% methyl-alcoholic hydrogen chloride (100 c.c.) for 4 hours. The mixture was poured into water and extracted with ether, the extract washed with sodium bicarbonate solution and dried, and the ether removed. The *methyl* ester crystallised from methyl alcohol in colourless prisms (9 g.), m. p. 72° (Found: C, 70·4; H, 6·0. $C_{19}H_{19}O_4N$ requires C, 70·2; H, 5·8%).

*β-Hydroxy-γ-phenoxy-α-phenylpropane.*—α-Phenoxyphenylacetone (Pfeiffer and Willems, *Ber.*, 1929, **62**, 1243) (1 g.) was gently boiled with aluminium *iso*propoxide (4·5 g.) in *iso*propyl alcohol (12 c.c.) and the acetone was removed through a short column. After 1 hour the solvent was removed under reduced pressure, and dilute hydrochloric acid added; the product, isolated with ether, crystallised from ether–light petroleum in hexagonal plates (0·8 g.), m. p. 92° (Found: C, 78·7; H, 7·0. $C_{15}H_{16}O_2$ requires C, 78·8; H, 7·0%).

*α-Cyano-β-keto-γ-phenoxy-α-veratrylpropane* was prepared by boiling veratrylacetonitrile (5·3 g.) and methyl phenoxyacetate (5 g.) with sodium ethoxide (from 0·7 g. of sodium) in alcohol (15 c.c.). After 2 hours, water was added, neutral matter removed with ether, and the alkaline liquor acidified. The *cyano-ketone*, isolated with ether, crystallised from aqueous methyl alcohol in colourless prisms (6 g.), m. p. 111—112° (Found: C, 69·7; H, 5·3. $C_{18}H_{17}O_4N$ requires C, 69·5; H, 5·5%).

*β-Keto-γ-phenoxy-α-veratrylbutyramide* was prepared by hydrolysing the above cyano-ketone (5 g.) with acetic acid (120 c.c.) and fuming hydrochloric acid (80 c.c.) in the cold. After 2 days, water was added, and some of the solvent removed under diminished pressure; the product crystallised from acetic acid in colourless needles (4·8 g.), m. p. 173° (Found: C, 65·7; H, 5·6. $C_{18}H_{19}O_5N$ requires C, 65·7; H, 5·8%), which gave a red-brown ferric test.

*γ-Phenoxy-α-veratrylacetone*, obtained in 60% yield by boiling the above amide for 6 hours with 8% hydrochloric acid (50 parts), crystallised from ether–light petroleum or a little methyl alcohol in slender prisms, m. p. 63—64° (Found: C, 71·4; H, 6·1. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%).

*β-Hydroxy-γ-phenoxy-α-veratrylpropane*, prepared by reducing the above ketone (1·4 g.) with aluminium *iso*propoxide (5 g.) in *iso*propyl alcohol (12 c.c.), separated from ether–light petroleum in compact prisms (1 g.), m. p. 100° (Found: C, 71·0; H, 6·9. $C_{17}H_{20}O_4$ requires C, 70·8; H, 7·0%).

*γ-Veratroyl-*n*-butyric Acid.*—Veratrole (6 g.) and glutaric anhydride (5 g.) were added to aluminium chloride (12 g.) in nitrobenzene (50 c.c.) at 0°. After 12 hours, dilute hydrochloric acid was added, the nitrobenzene removed in steam, and the solid residue collected after cooling. The crude acid was dissolved in sodium bicarbonate solution, recovered, dried, and crystallised from benzene; colourless prisms (5 g.), m. p. 140—142°, were obtained (Found: C, 61·6; H, 6·5. $C_{13}H_{16}O_5$ requires C, 61·9; H, 6·3%).

*δ-Veratrylvaleric acid*, obtained by heating the above keto-acid (1 g.) with concentrated hydrochloric acid (10 c.c.) and amalgamated zinc (5 g.) for 12 hours, crystallised from benzene in colourless small prisms (0·7 g.), m. p. 78° (Found: equiv., 239. $C_{13}H_{18}O_4$ requires equiv., 238).

King's College, Newcastle-upon-Tyne. [*Received, April 7th, 1938.*]

# 154. *The Constituents of Natural Phenolic Resins. Part XI. Synthesis of 2- and 3-Methyl-6 : 7-dimethoxy-1-veratrylnaphthalenes.*

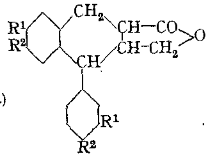
By Robert D. Haworth and David Woodcock.

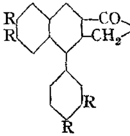
A further example of the irregular behaviour observed with lead tetra-acetate and members of the lignan group is reported. *l*-Conidendrin dimethyl ether (I; $R^1 = R^2 =$ OMe) is dehydrogenated by means of the tetra-acetate to (II; R = OMe) (J., 1935, 636), which is reduced by sodium amalgam to a racemic form of (I; $R^1 = R^2 =$ OMe). On treatment with lead tetra-acetate, this racemate loses hydrogen and carbon dioxide and is converted into 6 : *7-dimethoxy-1-veratryl-2-methylnaphthalene* (V), the structure of which has been established by an independent synthesis.

6 : 7-Dimethoxy-1-veratryl-3-methylnaphthalene (X; R = Me) has been prepared by an unambiguous method, and its identity with a substance in Part IX (J., 1937, 1647, 1648) confirms the structural suggestions advanced in the previous communication.

The action of lead tetra-acetate on lignan derivatives has been studied in several previous papers of this series. Usually dehydrogenation occurs and compounds of type (I) are converted into the corresponding naphthalene derivatives (II). The conversion of diarylbutanes of type (IV) into mixtures of naphthalene derivatives (II) and (III) has been observed with matairesinol dimethyl ether (IV; $R^1 = R^2 =$ OMe) and arctigenin ethyl ether (IV; $R^1 =$ OMe, $R^2 =$ OEt), and in the conversion of *O*-acetylarctigenin (IV; $R^1 =$ OMe, $R^2 = O{\cdot}CO{\cdot}CH_3$) into a monomethyl ether of conidendrin (I; $R^1 =$ OMe, $R^2 =$ OH) (Omaki, *J. Pharm. Soc. Japan*, 1937, 57, 22) the dehydrogenation is arrested at the tetrahydronaphthalene stage. Abnormal results have, however, been reported; the methylenedioxy-groups of hinokinin (IV; $R^1R^1 = R^1R^2 = CH_2O_2$) are attacked by the tetra-acetate and indefinite phenolic compounds are obtained, although in the case of anhydropicropodophyllin (J., 1936, 352) the methylenedioxy-groups do not interfere appreciably with the normal dehydrogenation reaction. The present work discloses a further abnormality observed with lead tetra-acetate.

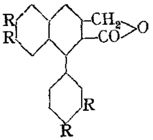
(I.)

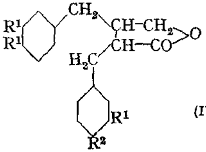




(II.)

(III.)

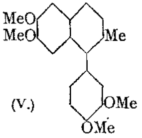




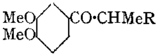
(IV.)

In the course of other experiments the lactone (II; R = OMe) of 6 : 7-dimethoxy-1-veratryl-2-hydroxymethylnaphthalene-3-carboxylic acid was reduced with sodium amalgam in boiling alkaline solution to a crystalline *lactone*, $C_{22}H_{24}O_6$, and, as this lactone was oxidised by sodium hypobromite to a mixture of 2-veratroylveratric acid and an acid whose methyl ester gave analytical figures in agreement with a racemic form of methyl 6 : 7-dimethoxy-1-veratryl-1 : 2 : 3 : 4-tetrahydronaphthalene-2 : 3-dicarboxylate, there can be little doubt that it represents one of the four theoretically possible racemates of conidendrin dimethyl ether (I; $R^1 = R^2 =$ OMe). Unlike the latter, which is

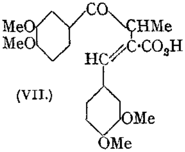
converted into (II; R = OMe) by the action of lead tetra-acetate, the racemate was dehydrogenated and decarboxylated to 6 : 7-*dimethoxy*-1-*veratryl*-2-*methylnaphthalene* (V). The structure of (V) was established by an independent synthesis from propioveratrone (VI; R = H), obtained by the action of propionyl chloride on veratrole.



(V.)

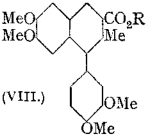


(VI.)

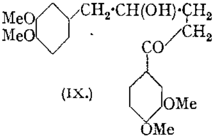


(VII.)

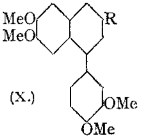
Bromination yielded α-*bromopropioveratrone* (VI; R = Br), which was converted into β-*veratroyl*-n-*butyric acid* (VI; R = $CH_2 \cdot CO_2H$) by condensation with ethyl sodiomalonate in the usual way. The sodium salt of (VI; R = $CH_2 \cdot CO_2H$) reacted with veratraldehyde to give the orange-coloured *lactone* of β-*veratroyl*-α-*veratrylidene*-n-*butyric acid* (VII). The acid (VII) has not been isolated in a pure condition, largely on account of the ease with which it undergoes lactonisation, but the methyl ester, prepared by the action of diazomethane on the crude acid, was converted into *methyl* 6 : 7-*dimethoxy*-1-*veratryl*-2-*methylnaphthalene*-3-*carboxylate* (VIII; R = Me) by the action of methyl-alcoholic hydrogen chloride. Decarboxylation of the corresponding *acid* (VIII; R = H) with quinoline and copper-bronze gave 6 : 7-dimethoxy-1-veratryl-2-methylnaphthalene (V), identical with the lead tetra-acetate dehydrogenation product of the racemate of conidendrin dimethyl ether.



(VIII.)



(IX.)



(X.)

In Part IX (J., 1937, 1646) veratryl γ-hydroxy-δ-veratrylbutyl ketone (IX; see this vol., p. 802) was converted into a compound for which structure (X; R = Me) was tentatively advanced : this suggestion has now been confirmed by an unambiguous synthesis. 6 : 7-Dimethoxy-1-veratrylnaphthalene-3-carboxylic acid (X; R = $CO_2H$) (J., 1935, 636) was converted into the *acid chloride* (X; R = COCl), which was reduced by Rosenmund's method to the *aldehyde* (X; R = CHO). The aldehyde gave amorphous products on attempted reduction by Clemmensen's method, but reduction to (X; R = Me) was effected by subjecting the *hydrazone* or *semicarbazone* to the Wolff–Kishner process. Demethylation occurred during the reaction, but subsequent methylation of the phenolic fraction with diazomethane gave small yields of 6 : 7-dimethoxy-1-veratryl-3-methylnaphthalene (X; R = Me), which was identical with the substance obtained as described in Part IX (*loc. cit.*). It is noteworthy that the conversion of (IX) into the naphthalene derivative (X; R = Me) is effected by the use of acidic cyclising agents and subsequent treatment with alkali, and dehydrogenating agents such as selenium, lead tetra-acetate, and palladium-black are not involved in the reaction.

## Experimental.

*Lactone of* 6 : 7-*Dimethoxy*-1-*veratryl*-2-*hydroxymethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*-3-*carboxylic Acid* (I; $R^1 = R^2$ = OMe).—The lactone of 6 : 7-dimethoxy-1-veratryl-2-hydroxymethylnaphthalene-3-carboxylic acid (II; R = OMe) (1 g.) (J., 1935, 1580) was refluxed with methyl alcohol (15 c.c.) and 10% potassium hydroxide solution (20 c.c.) until solution was complete. The alcohol was removed, water (30 c.c.) added, and the solution boiled for 6—7 hours during the gradual addition of 4% sodium amalgam (130 g.). The filtered solution was

acidified with dilute sulphuric acid, boiled for 1 hour, cooled, and extracted with chloroform. The extract, after being washed with sodium bicarbonate solution, was dried, and the solvent removed; the light brown residue (0·7 g.) crystallised from methyl alcohol (carbon) in colourless slender prisms (0·3 g.), m. p. 180° (Found: C, 69·1, 69·2; H, 6·3, 6·5. $C_{22}H_{24}O_6$ requires C, 68·8; H, 6·3%). A solution of bromine (0·8 c.c.) in 10% sodium hydroxide solution (20 c.c.) was added to a boiling solution of the lactone (I; $R^1 = R^2 =$ OMe) (1 g.) in N/2-sodium hydroxide (20 c.c.) and dioxan (10 c.c.). After boiling for 3 hours, the dioxan was removed and the products were separated as described in a similar case (J., 1937, 391). The lactonic fraction crystallised from methyl alcohol (carbon) in stout rhombic prisms, m. p. 205—206° (Found: C, 65·8; H, 6·1. $C_{22}H_{24}O_7$ requires C, 66·0; H, 6·0%); the figures correspond to a hydroxy-substitution product of the lactone (I; $R^1 = R^2 =$ OMe), but the product has not been fully examined. The acidic fraction on esterification yielded methyl 2-veratroylveratrate, m. p. 154—155°, which was identified by comparison with an authentic specimen, and a small amount of a *dimethyl* ester, which separated from a little methyl alcohol in colourless nodules, m. p. 148—149° (Found: C, 64·5; H, 6·6. $C_{24}H_{28}O_8$ requires C, 64·9; H, 6·4%).

6 : 7-*Dimethoxy-1-veratryl-2-methylnaphthalene* (V).—The above lactone (0·2 g.) and lead tetra-acetate (0·4 g.) were heated for ½ hour at 70—80° in glacial acetic acid (10 c.c.). Water was added; the product, isolated with chloroform and washed with sodium bicarbonate solution, was crystallised from methyl alcohol (carbon), and traces of lactonic matter were removed by boiling for 1 hour with 10% methyl-alcoholic potassium hydroxide and pouring into water. The *compound* (V), isolated with chloroform, separated from methyl alcohol–chloroform in stout prisms (0·09 g.), m. p. 141° (Found: C, 74·6; H, 6·8. $C_{21}H_{22}O_4$ requires C, 74·6; H, 6·5%).

*Propioveratrone* (VI; R = H).—The yields recorded by previous workers (Martegiani, *Gazzetta*, 1912, **42**, ii, 347; Johnson and Hodge, *J. Amer. Chem. Soc.*, 1913, **35**, 1022) were considerably improved by using nitrobenzene as solvent in the Friedel–Crafts reaction. Propionyl chloride (7 g.) was gradually added with cooling to a mixture of veratrole (12 g.) and aluminium chloride (16 g.) in nitrobenzene (40 c.c.). After 24 hours, dilute sulphuric acid was added, the nitrobenzene removed in steam, and the product isolated with ether and distilled. Propioveratrone, b. p. 137°/0·2 mm., crystallised from ether–light petroleum (1 : 5) in colourless cubes (12·5 g.), m. p. 59—60°. The semicarbazone separated from methyl alcohol in colourless prisms, m. p. 192—193° (Martegiani, *loc. cit.*, gives 190—192°).

α-*Bromopropioveratrone* (VI; R = Br).—Bromine (3·0 c.c.) in chloroform (9 c.c.) was gradually added to a solution of propioveratrone (11·6 g.) in chloroform (50 c.c.). After 4 hours, hydrogen bromide was removed in a stream of dry air, the chloroform was washed with sodium bicarbonate solution and dried, and the solvent removed. The residue, which solidified on trituration with ether, crystallised from ether–light petroleum (1 : 10) in long rectangular prisms (12 g.), m. p. 83—84° (Found: Br, 28·9. $C_{11}H_{13}O_3Br$ requires Br, 29·3%).

β-*Veratroyl*-n-*butyric acid* (VI; R = $CH_2 \cdot CO_2H$).—A solution of β-bromopropioveratrone (8·5 g.) in benzene (30 c.c.) was added to ethyl sodiomalonate (from 0·96 g. of sodium and 6·6 g. of ethyl malonate) in benzene (30 c.c.). After 3 hours' boiling, water was added, the benzene layer separated, and the solvent removed. The residual brown oil was boiled for 1 hour with 10% methyl-alcoholic potassium hydroxide (80 c.c.), the alcohol removed, a slight excess of dilute sulphuric acid added, and the product isolated with chloroform and heated at 180° for ½ hour. The crude *acid* (VI; R = $CH_2 \cdot CO_2H$) was taken up in sodium bicarbonate solution, recovered (6·0 g.), and crystallised from hot water (carbon), giving colourless prismatic plates, m. p. 129° (Found: C, 61·5, 61·6; H, 6·4, 6·5; equiv., 254. $C_{13}H_{16}O_5$ requires C, 61·9; H, 6·4%; equiv., 252).

*Lactone of* β-*Veratroyl*-α-*veratrylidene*-n-*butyric Acid* (VII).—A methyl-alcoholic solution of the above acid (VI; R = $CH_2 \cdot CO_2H$) (1·2 g.) was neutralised with sodium hydroxide and evaporated to dryness. The dry sodium salt, veratraldehyde (0·8 g.), and acetic anhydride (2 c.c.) were heated at 100° for 12 hours. After cooling, methyl alcohol was added and the product was collected, washed successively with water and a little methyl alcohol, and crystallised from methyl alcohol–chloroform; orange yellow prisms (1·0 g.), m. p. 183°, were obtained (Found: C, 69·4; H, 5·8. $C_{22}H_{22}O_6$ requires C, 69·1; H, 5·8%). This *lactone* was refluxed for ½ hour with a slight excess of sodium methoxide in methyl alcohol; water was added, and the alcohol removed. Acidification of the filtered solution yielded the crude acid (VII) as a white precipitate, m. p. 70—73°, which has not been crystallised. Attempts to cyclise this crude acid with methyl-alcoholic hydrogen chloride gave the yellow lactone, m. p. 183°.

**6 : 7-*Dimethoxy-1-veratryl-2-methylnaphthalene-3-carboxylic Acid*** (VIII; R = H).—This was

obtained in small yield by the action of cold acetic–hydrochloric acid on the crude acid described above, but better results were obtained by the following method. The crude acid (VII) (0·5 g.) was dissolved in ether (20 c.c.), dried with sodium sulphate, and treated with a solution of diazomethane (from 2 c.c. of nitrosomethylurethane) in ether (10 c.c.). After 4 hours, the solution was washed first with dilute hydrochloric acid and then with dilute sodium hydroxide solution, and dried, and the solvent removed. The residual oily methyl ester was refluxed for ½ hour with methyl-alcoholic hydrogen chloride (10 c.c.); *methyl* 6 : 7-*dimethoxy*-1-*veratryl*-2-*methylnaphthalene*-3-*carboxylate* (VIII; R = Me) separated on cooling and crystallised from methyl alcohol, containing a little chloroform, in cream-coloured needles (0·3 g.), m. p. 178° (Found: C, 69·7; H, 6·4. $C_{23}H_{24}O_6$ requires C, 69·7; H, 6·6%). Hydrolysis of this methyl ester with the calculated amount of methyl-alcoholic potassium hydroxide gave the *acid* (VIII; R = H), which separated from methyl alcohol–chloroform in colourless prisms, m. p. 252° (Found: C, 68·7; H, 6·0. $C_{22}H_{22}O_6$ requires C, 68·8; H, 5·8%). The acid (0·25 g.) was boiled for 2 hours with pure quinoline (2 c.c.) in the presence of a trace of copper powder. Ether was added, the copper removed by filtration, the filtrate washed several times with dilute hydrochloric acid and then with dilute sodium hydroxide solution, and the ether removed. The residue crystallised from methyl alcohol in stout prisms (0·19 g.), m. p. 140—141° (Found: C, 74·6; H, 6·7%), not depressed by 6 : 7-dimethoxy-1-veratryl-2-methylnaphthalene (V) obtained as described on p. 811.

6 : 7-*Dimethoxy*-1-*veratrylnaphthalene*-3-*carboxylic Acid Chloride* (X; R = COCl).—The acid (X; R = $CO_2H$) (1 g.) and thionyl chloride (2 c.c.) were refluxed for 1 hour. The excess of thionyl chloride was removed, the residue dissolved in benzene (10 c.c.) and filtered through a 3 cm. column of alumina, and the benzene evaporated. The *acid chloride* (X; R = COCl) (0·85 g.))separated from benzene in colourless needles, m. p. 183—184° (Found: C, 65·4; H, 5·1; Cl, 9·5. $C_{21}H_{19}O_5Cl$ requires C, 65·2; H, 4·9; Cl, 9·1%). The purification with alumina removes traces of sulphur compounds which otherwise inhibit the catalytic reduction described below.

6 : 7-*Dimethoxy*-1-*veratrylnaphthalene*-3-*aldehyde* (X; R = CHO).—A rapid stream of hydrogen was passed through a solution of the acid chloride (X; R = COCl) (0·85 g.) in boiling xylene (10 c.c.) containing 5% palladium–barium sulphate (0·5 g.). Estimation of the hydrogen chloride eliminated proved the reduction to be complete after 1 hour. The filtered solution was evaporated in a vacuum; the *aldehyde* crystallised from benzene in clumps of needles (0·65 g.), m. p. 163—164° (Found: C, 71·9; H, 5·5. $C_{21}H_{20}O_5$ requires C, 71·6; H, 5·7%). The *oxime*, prepared in alcoholic solution, crystallised from methyl alcohol in colourless rectangular prisms, m. p. 185° (Found: C, 68·7; H, 5·8. $C_{21}H_{21}O_5N$ requires C, 68·7; H, 5·7%). The *hydrazone*, obtained by refluxing for 12 hours an alcoholic solution of the aldehyde with excess of hydrazine hydrate, separated on cooling in rectangular prisms, which melted at 175—176°, resolidified, and melted again at 305—306° (Found: C, 68·8; H, 6·0. $C_{21}H_{22}O_4N_2$ requires C, 68·8; H, 6·0%). The *semicarbazone*, prepared in hot alcoholic solution, crystallised from alcohol in rosettes of colourless rectangular prisms, which melted at 223—224°, resolidified, and melted again at 308—309° (Found: C, 64·3; H, 5·4. $C_{22}H_{23}O_5N_3$ requires C, 64·5; H, 5·6%).

6 : 7-*Dimethoxy*-1-*veratryl*-3-*methylnaphthalene* (X; R = Me).—The hydrazone (0·4 g.) or semicarbazone (0·5 g.) described above was heated at 180° for 18 hours with a solution of sodium ethoxide (from 0·4 g. of sodium) in alcohol (18 c.c.). Water was added, neutral matter removed with chloroform, the alkaline solution acidified, and the crude phenol isolated with ether, dried and added to an ethereal solution of diazomethane (from 2·5 c.c. of nitrosomethylurethane). After 12 hours, the solution was washed successively with dilute hydrochloric acid and dilute sodium hydroxide solution, and the solvent removed. The residue was dissolved in a little alcohol and converted into the red picrate, which was collected and decomposed by shaking with dilute aqueous ammonia. The hydrocarbon, isolated with ether, was purified first by sublimation at 0·1 mm. and finally by crystallisation from light petroleum. 6 : 7-Dimethoxy-1-veratryl-3-methylnaphthalene (X; R = Me) was obtained in stout prisms (0·07 g.), m. p. 141° (Found: C, 74·6; H, 6·6%), not depressed by the specimen obtained previously (J., 1937, 1646). The *picrate*, prepared in alcoholic solution from (X; R = Me) obtained by either method, separated from alcohol in slender red needles, m. p. 133° (Found: C, 56·9; H, 4·1. $C_{21}H_{22}O_4,C_6H_3O_7N_3$ requires C, 57·1; H, 4·4%).

The following compounds were obtained during some preliminary experiments.

6 : 7-*Dimethoxy*-1-*veratryl*-3-*methyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*-2-*carboxylic Acid*.—Ethyl hydroxymethylenemethylsuccinate (Fichter and Rudin, *Ber.*, 1904, 37, 1611) (5 g.) and veratrole (6 g.) in acetic acid (20 c.c.) were gradually added with shaking to an ice-cold mixture

of concentrated sulphuric acid (30 c.c.) and acetic acid (30 c.c.). After 12 hours, water was added and the product, isolated with chloroform, was hydrolysed by boiling with 10% methyl-alcoholic potassium hydroxide (50 c.c.) for 2 hours. The alcohol was removed, water (25 c.c.) added, and hydrolysis completed by boiling for a further 2 hours. After acidification, the product, isolated with chloroform, was refluxed with acetyl chloride (10 c.c.) for 1 hour, and the excess of the latter removed. The oily residue (4 g.), dissolved in nitrobenzene (10 c.c.), was added with shaking to an ice-cold solution of aluminium chloride (6 g.) in nitrobenzene (30 c.c.); after 12 hours, dilute hydrochloric acid was added, and the nitrobenzene removed in steam. Without purification the crude keto-acid (3·5 g.), isolated with chloroform, was reduced by boiling with amalgamated zinc (15 g.) and concentrated hydrochloric acid (20 c.c.) for 12 hours; 6 : 7-*dimethoxy*-1-*veratryl*-3-*methyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*-2-*carboxylic acid*, isolated with chloroform, separated from benzene in colourless nodules (0·5 g.), m. p. 220—222° (Found: C, 68·3; H, 7·0. $C_{22}H_{26}O_6$ requires C, 68·4; H, 6·7%). Attempts to decarboxylate this acid were unsuccessful.

6 : 7-*Dimethoxy*-1-*veratryl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*-3-*carboxylic Acid*.—4% Sodium amalgam (120 g.) was gradually added to a boiling solution of 6 : 7-dimethoxy-1-veratryl-naphthalene-3-carboxylic acid (1 g.) (J., 1935, 640) in 10% potassium hydroxide solution (30 c.c.). After 6 hours, the filtered solution was acidified, and the product collected. The *acid* crystallised from methyl alcohol in colourless needles (0·65 g.), m. p. 133°, containing one molecule of water of crystallisation (Found: C, 64·7; H, 6·5. $C_{21}H_{24}O_6,H_2O$ requires C, 64·6; H, 6·7%). The anhydrous acid crystallised from benzene in small needles, m. p. 170° (Found: C, 67·7; H, 6·5. $C_{21}H_{24}O_6$ requires C, 67·7; H, 6·5%). The *methyl* ester, prepared by the action of methyl-alcoholic hydrogen chloride, separated from methyl alcohol in rosettes of slender needles, m. p. 143—144° (Found: C, 68·1; H, 6·5. $C_{22}H_{26}O_6$ requires C, 68·4; H, 6·7%).

King's College, Newcastle-upon-Tyne. [*Received, April 7th*, 1938.]

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## 155. *A Comparison of the Rates of Formation of Six- and Seven-membered Ring Compounds from ω-Chloro-sulphides.*

By G. M. Bennett and (Miss) E. G. Turner.

The rates of formation in solution of cyclic sulphonium salts, from alkyl sulphides having a chlorine atom attached to the last carbon atom of the chain, have been studied for compounds yielding six- and seven-membered ring products. The reaction is in each case smooth and of the first order, and the six-membered ring is found to be formed 75 times as fast as the seven-membered. This ratio is almost identical with that found in an earlier study for the ratio of the speeds of formation of five- and six-membered rings of similar type. Although these reactions appear in general to proceed to completion, the possibility is noted that they are reversible and incomplete.

In an earlier paper (Bennett, Heathcoat, and Mosses, J., 1929, 2567) an account was given of the formation of compounds containing five- and six-membered heterocyclic rings from ω-chloro-sulphides. The phenyl ω-chloroalkyl sulphides underwent ring closure smoothly at measurable speeds. Of the alkyl ω-chloroalkyl sulphides, that giving rise to the five-membered ring reacted too rapidly for measurement. It was shown that the speeds of ring closure of a five- and a six-membered ring in 50% acetone solution at 80° were in the ratio of 76 : 1.

We now report a similar study of substances yielding six- and seven-membered ring compounds. An examination of *phenyl 6-chlorohexyl sulphide* showed that, heated in various solvents at temperatures up to 200°, it either gave no sign of cyclisation or did so to a minor extent. This was not surprising in view of the difficulty of closure of a seven-membered ring which is here superposed upon the known slowness of reaction of alkyl chlorides with the sulphur atom when directly attached to the benzene nucleus. *Ethyl 6-chlorohexyl sulphide*, however, undergoes ring closure smoothly under these

conditions and rapidly enough for study in comparison with the corresponding *ethyl 5-chloroamyl sulphide*. In each case the reaction appears to be of the first order, and the speed of formation of the six-membered ring is found to be about 75 times as great as that of the seven-membered. The replacement of the methyl group attached to the sulphur atom by an ethyl group caused a fall in velocity of ring closure in the ratio 3 : 2.

As in the earlier work, the observations have been made at two temperatures, but the uncertainty as to whether the reaction is really complete, in view of the known reversibility of sulphonium-salt formation, makes a more detailed examination of each reaction desirable before the results could safely be used to calculate the activation energy of the reaction. At the same time, any reversal of the reaction is slight, and the observed velocities are not seriously in error.

## Experimental.

*Attempt to detect Ring Closure in Phenyl 6-Chlorohexyl Sulphide.*—The substance, prepared as described by Bennett and Mosses (J., 1931, 1699), gave no sign of chlorion formation after 29 hours' heating in boiling 70% acetic acid or after 26 hours in boiling 70% aqueous acetone. After 72 hours in the latter solvent, liberation of chlorion was 13% of that possible. The substance was also heated in ethylene glycol at its b. p. (198°); after 16 hours the liberated chlorion was 25% of that possible. As both hydrolysis and glycolysis were probable alternative reactions involving liberation of hydrogen chloride, these figures in any case only indicate an upper limit to the extent of any ring formation occurring.

*Preparation of Hexamethylene Chlorohydrin.*—This substance had not hitherto been prepared, Bennett and Mosses having made use of the chloroacetin. Hexamethylene glycol was subjected to the action of hydrochloric acid in the presence of paraffin under the special conditions described by Bennett and Mosses (*loc. cit.*, p. 1698), and, after repeated fractional distillation under diminished pressure, finally with a glass spiral column, *hexamethylene chlorohydrin* was obtained as a colourless liquid, b. p. 116—117°/19 mm., 112°/17 mm. (Found: C, 53·1; H, 9·5; Cl, 26·2. $C_6H_{13}OCl$ requires C, 52·7; H, 9·6; Cl, 26·0%).

*Preparation of Ethyl 6-Chlorohexyl Sulphide.*—Potassium ethylthioxide was heated for ½ hr. with hexamethylene chlorohydrin in alcoholic solution, and after passage of steam to remove volatile material, the ethyl hydroxyhexyl sulphide was removed in ether, dried with potassium carbonate, and distilled, forming a colourless oil, b. p. 134—136°/17 mm. This hydroxy-sulphide (6·5 g.), dissolved in diethylaniline (8·6 c.c.), was kept at 55° while thionyl chloride (3·7 c.c. in an equal volume of carbon tetrachloride) was added drop by drop. After a further ¾ hr.'s heating on the steam-bath, water and more carbon tetrachloride were added, and the extract washed twice with hydrochloric acid and then successively with dilute sodium carbonate solution and with water and dried over sodium sulphate. On distillation there was thus obtained *ethyl 6-chlorohexyl sulphide* as a pale straw-coloured oil of persistent unpleasant odour; b. p. 128—131°/26 mm. (Found: C, 53·4; H, 9·4; Cl, 19·6. $C_8H_{17}ClS$ requires C, 53·2; H, 9·9; Cl, 19·7%).

Ethyl chlorohexyl sulphide was heated in 50% aqueous acetone solution in a sealed tube at 100° for 90 hrs., and the solution diluted and extracted with ether to remove any unchanged oil. The solution was then concentrated and chloroplatinic acid added.

*Ethylhexamethylenesulphonium chloroplatinate*, $[Et{\cdot}S(CH_2)_6]_2PtCl_6$, was thus obtained in yellow crystals somewhat readily soluble in water (Found: C, 27·8; H, 4·9; Pt, 27·5. $C_{16}H_{34}Cl_6S_2Pt$ requires C, 27·9; H, 4·6; Pt, 27·5%).

*Preparation of Ethyl 5-Chloroamyl Sulphide.*—The corresponding hydroxy-sulphide was obtained by boiling 5-chloroamyl acetate (18 g.) with an aqueous-alcoholic solution of potassium ethylthioxide (8·5 c.c. of ethylthiol with 6·5 g. of potassium hydroxide in 20 c.c. of 60% alcohol) for ½ hr., and heating for a further ½ hr. after addition of more potassium hydroxide (2 mols.). The alcohol was evaporated, the mixture cooled, the oily layer removed, the liquor extracted with ether, and the combined extracts dried over potassium carbonate. On distillation, 12·4 g. of ethyl 5-hydroxyamyl sulphide, b. p. 135°/20 mm., were obtained.

To this hydroxy-sulphide, dissolved in 15 c.c. of diethylaniline at 50—60°, thionyl chloride (6·25 c.c. in an equal volume of carbon tetrachloride) was added drop by drop, and the mixture heated for 1 hr. on the steam-bath. After addition of water the product was collected in carbon tetrachloride and the extract washed twice with hydrochloric acid and then successively with aqueous sodium carbonate and with water and dried over sodium sulphate. Distillation yielded *ethyl 5-chloroamyl sulphide* as a pale yellow oil of characteristic and

persistent odour; b. p. 122°/25 mm. (Yield 64% of the calculated) (Found: C, 50·9; H, 9·2. $C_7H_{15}SCl$ requires C, 50·5; H, 9·1%).

When an aqueous acetone solution of this sulphide which had been boiled for several hours was evaporated, some unchanged oil removed in ether, and the aqueous solution further concentrated, it yielded on addition of chloroplatinic acid *ethylpentamethylenesulphonium chloroplatinate* in orange-yellow crystals readily soluble in water (Found: Pt, 28·8. $C_{14}H_{30}Cl_6S_2Pt$ requires Pt, 29·1%).

*Reaction-velocity Measurements.*—Equal volumes of an M/20-solution of the chloro-sulphide in acetone were placed in each of a number of glass tubes, an equal volume of water added, and the tube sealed and heated at constant temperature. A tube was removed and opened at certain intervals of time and the chlorion in solution was determined gravimetrically as silver salt. Time was measured in minutes, and $k$ is calculated from $k = (1/t) \log_e a/(a - x)$.

(a) *Closure of the seven-membered ring.*

(1) Each tube contained 20 c.c. of 50% aqueous acetone with 0·09188 g. of ethyl 6-chlorohexyl sulphide. Temp. 100·0°.

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| $t$, mins. ........... | 0 | 300 | 420 | 480 | 600 | 900 | 1080 | 1500 | ∞ |
| AgCl, g. ........... | — | 0·0150 | 0·0183 | 0·0201 | 0·0274 | 0·0339 | 0·0371 | 0·0459 | 0·0730 |
| $k \times 10^4$ ........... | — | 7·68 | 6·87 | 6·72 | 7·83 | 6·95 | 6·57 | 6·60 | Mean 7·03 |

(2) As in (1), except that the concentration was halved.

| | | | | | |
|---|---|---|---|---|---|
| $t$, mins. ........... | 0 | 480 | 600 | 900 | ∞ |
| AgCl, g. ........... | — | 0·0102 | 0·0141 | 0·0184 | 0·0365 |
| $k \times 10^4$ ........... | — | 6·83 | 8·15 | 7·78 | Mean 7·58 |

(3) 20 C.c. of 50% aqueous acetone with 0·07648 g. of sulphide. Temp. 116·0°.

| | | | | | |
|---|---|---|---|---|---|
| $t$, mins. ........... | 0 | 180 | 240 | 360 | ∞ |
| AgCl, g. ........... | — | 0·0237 | 0·0293 | 0·0376 | 0·06075 |
| $k \times 10^4$ ........... | — | 27·4 | 27·4 | 26·8 | Mean 27·2 |

(b) *Closure of the six-membered ring.*

(1) Each tube contained 20 c.c. of 50% aqueous acetone with 0·08415 g. of ethyl 5-chloroamyl sulphide. Temp. 68·6°.

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| $t$, mins. ........... | 0 | 15 | 45 | 75 | 105 | 135 | 165 | 195 | ∞ |
| AgCl, g. ........... | — | 0·0052 | 0·0124 | 0·0210 | 0·0274 | 0·0325 | 0·0382 | 0·0416 | 0·0725 |
| $k \times 10^3$ ........... | — | — | 4·68 | 4·56 | 4·51 | 4·40 | 4·54 | 4·38 | Mean 4·51 |

(2) As in (1). Temp. 80·4°.

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| $t$, mins. ........... | 0 | 15 | 30 | 40 | 50 | 60 | 70 | 90 | ∞ |
| AgCl, g. ........... | — | 0·0111 | 0·0194 | 0·0248 | 0·0299 | 0·0361 | 0·0396 | 0·0442 | 0·0725 |
| $k \times 10^3$ ........... | — | 11·06 | 10·39 | 10·46 | 10·88 | 11·50 | 11·28 | 10·46 | Mean 10·8 |

(3) Each tube contained 20 c.c. of 50% aqueous acetone with 0·0828 g. of ethyl 5-chloroamyl sulphide. Temp. 88·6°.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| $t$, mins. ........... | 0 | 10 | 15 | 20 | 25 | 30 | ∞ |
| AgCl, g. ........... | — | 0·0147 | 0·0204 | 0·0264 | 0·0289 | 0·0349 | 0·0690 |
| $k \times 10^3$ ........... | — | 24·0 | 23·3 | 24·2 | 21·6 | 23·5 | Mean 23·3 |

Extrapolating the figures for the closure of the six-membered ring from 68·6° and 88·6°, we get $k_{100°} = 0·0530$.

The ratio of velocities of closure of six- and seven-membered rings at 100° is therefore 0·0530/0·000703 = 75.

THE UNIVERSITY, SHEFFIELD. [*Received, March 31st, 1938.*]

## 156. *The Acid–Base Function in Non-aqueous Media. Part I. The Autoprotolytic Constant of* m-*Cresol.*

By D. C. GRIFFITHS.

A potentiometric method, similar to that used in the classical researches on the determination of the autoprotolytic constant of water, has been devised for measurements with *m*-cresol. The effect of small concentrations of water is considered.

ACCORDING to the new theory of acids and bases, first clearly stated by Brönsted (*Rec. Trav. chim.*, 1923, **42**, 718; *J. Physical Chem.*, 1926, **30**, 777), the fundamental reaction in all acid–base equilibria is not dissociation but protolysis. In a pure hydrolytic solvent such a reaction can proceed automatically; for instance, in the case of water the reaction can be represented by the equation

$$2H_2O = H_3O^+ + OH^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and the process is called " autoprotolysis."

The law of mass action is applied to this reaction and the active mass of the neutral water is assumed constant. Then, by definition, the autoprotolytic constant of water is given by

$$K_W = c_{H_3O^+} \cdot c_{OH^-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Recent studies on the behaviour of acids and bases in *m*-cresol (Brönsted, Delbanco, and Tovborg-Jensen, *Z. physikal. Chem.*, 1934, **169**, 361) indicate that this solvent enters into protolytic reactions with the acids (HA) and bases (B):

$$HA + CH_3 \cdot C_6H_4 \cdot OH = CH_3 \cdot C_6H_4 \cdot OH_2^+ + A^- \quad . \quad . \quad . \quad . \quad . \quad (3)$$
$$B + CH_3 \cdot C_6H_4 \cdot OH = CH_3 \cdot C_6H_4 \cdot O^- + BH^+ \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Autoprotolysis is a special case of such equilibria, and it is logical to assume that it occurs in *m*-cresol:

$$2CH_3 \cdot C_6H_4 \cdot OH = CH_3 \cdot C_6H_4 \cdot OH_2^+ + CH_3 \cdot C_6H_4 \cdot O^- \quad . \quad . \quad . \quad . \quad (5)$$

for which the autoprotolytic constant is given by

$$K_{W\,(cresol)} = c_{CH_3 \cdot C_6H_4 \cdot OH_2^+} \cdot c_{CH_3 \cdot C_6H_4 \cdot O^-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

In the present work this constant has been measured by a method similar to one of those employed for the same determination in the case of water. Use is made of the fact that the concentration of hydrogen ions in an alkaline solution can be determined by measuring the *E.M.F.* of an acid–alkali cell (Ostwald, *Z. physikal. Chem.*, 1893, **11**, 521; Arrhenius, *ibid.*, p. 805; Loewenherz, *ibid.*, 1894, **14**, 155).

In a cell of the type represented by the scheme

$$H_2 \mid \text{acid solution} \mid \text{base solution} \mid H_2$$

the *E.M.F.* is given by

$$E = 0{\cdot}057 \log c_a/c_b \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where $c_a$ and $c_b$ represent the solvated hydrogen-ion concentrations on the acid and the base side, respectively, if the complications due to diffusion and liquid–liquid junction potentials are ignored. Attention must be paid to the elimination or minimisation of these factors, and at the same time it is desirable to increase the conductivity of the system. This can be brought about by the use of a suitable salt solution as medium (see p. 817).

In the equations (3) and (4), if the acid HA or the base B is sufficiently strong, the reactions proceed to the right almost completely: in the present work HA was a strong organic acid and B a strong organic base. If, however, the base is not sufficiently strong in *m*-cresol, reaction (4) does not proceed completely from left to right and the concentration of the ion $CH_3 \cdot C_6H_4 \cdot O^-$ is given by $c_B p/100$, where $p$ is the percentage protolysis. Professor Brönsted (private communication), by conductivity measurements, has found the protolysis of 0·01*m*-*iso*amylamine to be *ca.* 30% in *m*-cresol. Direct evidence on the absolute strength of benzenesulphonic acid in *m*-cresol is lacking, but such evidence as there is (Brönsted and Volqvartz, private communication), which is based on conductivity determinations of benzenesulphonates, indicates that this acid is very strong compared with trichloroacetic acid.

In the present investigation the *E.M.F.* of the cell

$$H_2 \mid 0{\cdot}01m\text{-benzenesulphonic acid} \mid 0{\cdot}01m\text{-piperidine} \mid H_2$$

(all in 0·1*m*-*iso*amylamine benzenesulphonate in *m*-cresol) was measured. The reactions concerned are represented by the equations

$$C_6H_5{\cdot}SO_2{\cdot}OH + CH_3{\cdot}C_6H_4{\cdot}OH = CH_3{\cdot}C_6H_4{\cdot}OH_2^+ + C_6H_5{\cdot}SO_2{\cdot}O^-$$
$$C_5H_{10}{>}NH + CH_3{\cdot}C_6H_4{\cdot}OH = CH_3{\cdot}C_6H_4{\cdot}O^- + C_5H_{10}{>}NH_2^+$$

The concentration of the solvated hydrogen ion is given by that of the acid added; that of the solvated hydrogen ion in the basic solution can then be calculated by use of equation (7).

## Experimental.

*Purification of Reagents.*—Benzenesulphonic acid was recrystallised from water, collected on a Buchner funnel surrounded by ice, and dehydrated at 50° over phosphoric oxide under reduced pressure. Analysis by titration against standard base indicated that less than 0·03 mole of water was present per mole of acid.

*iso*Amylamine benzenesulphonate was prepared by mixing the components in equivalent amounts, *viz.*, 32 g. of acid and 15 g. of base. The product was dissolved in alcohol, cooled, and reprecipitated by addition of ether. This operation was repeated, 13·5 g. of the salt being obtained.

Kahlbaum's *m*-cresol was shaken with solid sodium hydroxide, the liquid decanted into a bottle containing phosphoric oxide and again well shaken, and then distilled in an all-glass apparatus from a suspension of the dehydrating agent.

The cell used consisted of a U-tube somewhat constricted near the bends, stoppered at both ends, and provided also with an entry and an exit tube for hydrogen. A pair of platinum electrodes passed through each stopper. They were carefully insulated from each other, and in this way the potential of any electrode could be compared with each of the others in turn. (I am indebted to Mr. E. Guntelberg for suggesting this arrangement.) By this method any individual eccentricity of an electrode could be detected. The potentiometer was of the direct reading type, standardised by a Weston cell. "Electrolytic hydrogen" from a cylinder was passed over heated copper, bubbled through concentrated sulphuric acid, and finally passed through dry *m*-cresol. The stream of gas was equally divided.

The electrodes were tested in hydrochloric acid, and hydrogen passed through until the differences were of the order of 0·001 volt. The electrodes were replatinised several times during the course of the experiments. Great care was taken to remove the platinising liquor. After equilibrium had been attained in acid solution in water, the electrodes were well washed in water and then in alcohol and ether or in dry *m*-cresol. Both methods gave the same results. In acid solutions in *m*-cresol maximum differences of 0·002 volt were noted, and in basic solution in the same solvent maximum differences of 0·005 volt.

In a typical experiment 100 c.c. of 0·1*m*-*iso*amylamine benzenesulphonate were prepared, and 15 c.c. portions of 0·01*m*-benzenesulphonic acid and of piperidine severally were made up in this salt solution. A few c.c. of the *iso*amylamine benzenesulphonate solution were introduced into the cell, and clean dry sand was carefully added in such a way that no air bubbles were embedded in the mass. Sand was added until the viscous mass came up to the level of the constrictions in the cell. The excess of solution was removed with filter-paper. The sand bridge effectively prevented appreciable diffusion. Equal measured amounts of the 0·01*m*-benzenesulphonic acid solution and of the 0·01*m*-piperidine solution were poured simultaneously into the two halves of the cell.

The following is a record of the readings (in volts) obtained at various times with different electrodes.

| Electrodes. | 60 mins. | 80 mins. | 100 mins. |
|---|---|---|---|
| 4 . . . . . . . 1 | 0·5750 | 0·5757 | 0·5752 |
| 4 . . . . . . . 2 | 0·5752 | 0·5752 | 0·5759 |
| 3 . . . . . . . 1 | 0·5760 | 0·5762 | 0·5758 |
| 3 . . . . . . . 2 | 0·5760 | 0·5757 | 0·5755 |

Mean value of *E.M.F.* 0·575 volt.

Next, the basic solution was removed by a pipette and replaced by fresh basic solution.

After (*a*) 45 mins. and (*b*) 90 mins., the readings were as tabulated below. When the acid side was similarly replenished, the readings were (*c*) after a 45-mins. interval.

| Electrodes. | (*a*). | (*b*). | (*c*). |
|---|---|---|---|
| 4 . . . . . . . 1 | 0·5720 | 0·5720 | 0·5840 |
| 4 . . . . . . . 2 | 0·5728 | 0·5720 | 0·5842 |
| 3 . . . . . . . 1 | 0·5720 | 0·5717 | 0·5820 |
| 3 . . . . . . . 2 | 0·5718 | 0·5715 | 0·5820 |

The results may be summarised as below, the bridge in each experiment being a 0·1*m*-salt solution :

| | | |
|---|---|---|
| Expt. | 1 | 2 |
| Temp. | 23° | 19° |
| Soltn. 1 : Concn. (*m*) of $Ph\cdot SO_3H$ in 0·1*m*-salt soltn. | $10^{-2.22}$ | $10^{-1.89}$ |
| ,, 2 : ,, ,, $C_5H_{11}N$ ,, ,, ,, | $10^{-1.96}$ | $10^{-1.91}$ |
| Mean value of *E*, volt | 0·575 | 0·584 |
| *K* | $10^{-14.66}$ | $10^{-14.41}$ |

In the evaluation of the constants (*K*) it was assumed that the protolysis of the base was 30% and that of the acid 100%.

In order to determine if a small concentration of water in the *m*-cresol had much effect on the *E.M.F.* measurements, the following preliminary measurements were carried out. A uniform solution of benzenesulphonic acid was added to each side of the sand bridge. When a solution of water in *m*-cresol was added to one side of the cell until the concentration of water on this side was 0·01*m*, the change in *P.D.* was less than a millivolt. With a concentration as high as 0·05*m*, the difference only amounted to about 0·002 volt. Under the conditions of the final experiments no definite regularities could be found when successive drops of a solution of water in *m*-cresol were added, but since the influence of water is clearly so small, such effects do not have much bearing on the accuracy of the measurement of the autoprotolytic constant.

The values of the constant are strictly only valid under the given conditions of concentration and temperature. It is regarded as significant that the figures obtained are very nearly the same as those obtained for water under similar conditions. In this investigation salt effects have not been considered. These can only be studied when data over a much wider range of concentration have been collected. It is considered outside the scope of this paper to consider to what extent the ions associate to form electrostatic molecules.

This investigation was undertaken at the suggestion of Professor J. N. Brönsted, and throughout, his counsel and guidance were placed freely at my disposal. To him and also to the staff of this Institute, I wish to express my sincerest thanks.

UNIVERSITETETS FYSISK-KEMISKE INSTITUT,
COPENHAGEN, DENMARK.
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## 157. *The Acid–Base Function in Non-aqueous Media. Part II. The Relative Strengths of Acids in Chlorobenzene.*

By D. C. GRIFFITHS.

An indicator method has been used for the determination of the relative strengths of a number of organic acids in the solvent chlorobenzene. It has been found that there is for uncharged acids a very close parallelism between the relative strengths in water and those in chlorobenzene. Measurements have been made at (*a*) constant salt concentration and (*b*) constant "total acid" concentration. It has been found possible to allow for association by the method of LaMer and Downes.

ACCORDING to the classical ionisation theory of acids and bases, these exercised their functions when they gave rise respectively to hydrogen and to hydroxyl ions. Chlorobenzene is non-polar and non-ionising in the accepted sense, and there is certainly no way in which a base such as ammonia could on the classical theory exercise its basic function in chlorobenzene.

The situation was clarified by Brönsted's suggestion (*Rec. Trav. chim.*, 1923, **42**, 718; *J. Physical Chem.*, 1926, **30**, 777) that acids and bases could be defined by the relation Acid = Base + Proton. Later he gave an expression (*Ber.*, 1928, **61**, 2049) which serves as a measure of relative acidity in a given solvent. For the reaction represented by the equation, HA + B = HB + A, where B is a base, chosen as standard for the solvent employed, HA the acid used, HB the acid corresponding to the base B, and A the base corresponding to the acid HA, $K = c_{HB}c_A/c_Bc_{HA}$ serves as a measure of acidity in a given solvent. Already this has led to interesting results: not only has it been found possible to get a qualitative picture of the function of acids and bases in aprotic media, but investigation has started on the quantitative measurement of the relative strengths of acids and bases in such media. Brönsted (*loc. cit.*) made preliminary qualitative measurements of the order of the strengths of several indicators and acids in benzene, and LaMer and Downes (*Chem. Reviews*, 1933, **13**, 47) carried out more quantitative work in the same solvent.

In the investigation described below, a solvent of considerably higher dielectric constant than benzene (2·26) was chosen. (For a discussion of the effect of dielectric constant on the association of solutes, see Fuoss and Kraus, *J. Amer. Chem. Soc.*, 1933, **55**, 2387.) Chlorobenzene has a dielectric constant of 10·95, but in spite of this the effect of association is quite marked, and it is possible to apply the method of LaMer and Downes in the interpretation of the results.

The relative strengths of a wide series of organic acids have been measured, and the results are fully in conformity with the view predicted by theory that the order and, apart from small deviations, the relative numerical values of the strengths of these acids in chlorobenzene are the same as in water. Owing to the insolubility of their salts in chlorobenzene it was not possible to compare the relative strengths of bases in this solvent as, for instance, has been done in *m*-cresol (Brönsted, Delbanco, and Tovborg-Jeusen, *Z. physikal. Chem.*, 1934, **169**, 361).

## EXPERIMENTAL.

*Purification of Reagents.*—Commercially pure chlorobenzene was shaken with 10% sodium hydroxide solution, washed, shaken with dilute sulphuric acid, again washed, dried over phosphoric oxide, and distilled in an all-glass apparatus at low pressure. After use it was repurified by the same process. The other reagents had been purified by previous workers in this laboratory.

*Selection of Indicators.*—Preliminary semi-quantitative experiments were first made to determine the suitability of different indicators to be employed as indicated below. In order to compare the strength of an acid with that of an indicator, the experimental requirements were the determinations of the ratios of the concentrations of the acid and base forms of the indicator ($c_{HB}$ and $c_B$) and of the acid and base forms of the acid ($c_{HA}$ and $c_A$) in various acid-base mixtures. The equilibrium studied was

| HA | + | B | = | HB | + | A |
|---|---|---|---|---|---|---|
| Acid | | Base of indicator | | Acid of indicator | | Base of acid |

The concentration of the base, *e.g.*, $C_6H_5\cdot COO^-$, is fixed if the titration base B′ is sufficiently strong to convert its equivalent of benzoic acid into the benzoate ion: $B' + C_6H_5\cdot CO_2H = C_6H_5\cdot COO^- + B'H^+$. The concentration of the free acid was found simply by difference.

If one form of the indicator is colourless, the relative concentration of the two forms follows simply from the measurement of the extinction coefficients at suitable wave-lengths. When both forms show an absorption at all wave-lengths, but the relative extinction is widely different at some wave-lengths, then measurements are still possible, and the algebraic relationships are only a little more complicated. The indicators found suitable for use in the present investigation were 2 : 6-dinitrophenol and bromophenol-blue.

*Experiments with 2 : 6-Dinitrophenol.*—This indicator, in chlorobenzene as in water, exists in two forms, one coloured and one colourless, *viz.*, $C_6H_3(NO_2)_2\cdot O^-$ and $C_6H_3(NO_2)_2\cdot OH$, respectively. A solution of the indicator in chlorobenzene is turned yellow on addition of a drop of a strong base. By adding sufficient quantities of a strong base, such as *iso*butylamine, in small amounts, a solution of constant molecular absorption was obtained. This was a solution of the indicator in the completely yellow basic form. In the absorption measurements

a Pulfrich–Zeiss colorimeter, and in some cases also a Hilger spectrophotometer, was used. The former instrument was graduated to give directly the percentage of light transmitted by the indicator solutions at the different wave-lengths of the colour filters. The molecular extinction coefficients are given by the relation $\varepsilon_m = \log D/lm$, where $l$ is the length (in cm.) of the containing vessel, $m$ the molar concentration of the indicator, and $D$ the fraction of light transmitted.

It was not necessary to find the absolute values of the extinction coefficients, for, in a solution containing both forms of which one shows no absorption at the particular wave-length selected, the ratio of the molecular concentrations of the two forms is given by

$$c_{HB}/c_B = (\log D_2 - \log D_1)/(-\log D_1)$$

if the lengths of the tubes are the same, where $D_1$ is the fraction of light transmitted by the solution when the indicator is completely in the basic form, and $D_2$ that measured. In the above expressions Beer's law is assumed. For the ranges of concentration studied, the deviations were well within the limits of experimental error.

In each experiment the actual values of $D$ for the completely yellow solution were determined, rather than the alternative procedure of evaluating it from previous absorption measurements.

An approximately $10^{-4}$ *m*-solution of the indicator was made by dissolving about 0·05 g. in 25 c.c. of pure chlorobenzene and diluting 1 g. of this solution 100-fold by weighing. All the acid and base solutions employed were made up in this indicator solution : there was therefore no doubt about the constancy of the total indicator concentration.

In the experiments, 1·50—3·00 c.c. portions of 0·01*m*-*iso*butylamine were measured from a burette into a series of tubes, and sufficient acid solution (of appropriate concentration) was added to cause a visible diminution in the yellow colour of the solution. Readings of the value of $D$ at 4300 A. (the wave-length of the light transmitted by the yellow colour filter) were taken for a series of mixtures into which various quantities of the acid solution had been measured. The results for a number of acids are tabulated below.

The following symbols are used for the substances concerned in the equilibrium $A_1 + I_B = B_1 + I_A$ : $A_1$ is the titration acid, $B_1$ its conjugate base (in all the cases considered $B_1$ is the negative ion of the salt of $A_1$), $I_B$ is the basic (yellow) form of the indicator, $I_A$ the colourless acid form, and $B_2$ the titration base (*iso*butylamine).

### *Propionic acid.*

Mixtures : $A_1$ = 0·0606*m* ; $B_2$ = 0·01202*m*.

| $A_1$, c.c. | $B_2$, c.c. | $[A_1]$. | $[B_1]$. | D, %. | log $[I_B]/[I_A]$. | log $[B_1]/[A_1]$. |
|---|---|---|---|---|---|---|
| | | Yellow form | | 17·8 | | |
| 5·00 | 1·50 | 0·0438 | 0·00277 | 48·7 | −0·148 | −1·199 |
| 7·00 | 1·50 | 0·0478 | 0·00212 | 54·5 | −0·265 | −1·325 |
| 8·00 | 1·50 | 0·0491 | 0·00190 | 60·8 | −0·392 | −1·412 |
| 10·00 | 1·50 | 0·0511 | 0·00157 | 65·0 | −0·479 | −1·513 |

### *Acetic acid.*

Mixtures : $A_1$ = 0·0218*m* ; $B_2$ = 0·01060*m*.

| $A_1$, c.c. | $B_2$, c.c. | $[A_1]$. | $[B_1]$. | D, %. | log $[I_B]/[I_A]$. | log $[B_1]/[A_1]$. |
|---|---|---|---|---|---|---|
| | | Yellow form | | 17·9 | | |
| 2·50 | 1·50 | 0·00965 | 0·00397 | 21·6 | 0·909 | −0·386 |
| 3·00 | 1·50 | 0·01100 | 0·00353 | 22·2 | 0·847 | −0·494 |
| 5·00 | 1·50 | 0·0143 | 0·00245 | 31·1 | 0·335 | −0·766 |
| 7·00 | 1·50 | 0·0161 | 0·00187 | 41·1 | 0·033 | −0·935 |
| 8·00 | 1·50 | 0·0166 | 0·00168 | 43·5 | −0·027 | −0·995 |
| 10·00 | 1·50 | 0·0176 | 0·00138 | 51·0 | −0·192 | −1·106 |

### *Benzoic acid.*

Mixtures : $A_1$ = 0·0100*m* ; $B_2$ = 0·01038*m*.

| $A_1$, c.c. | $B_2$, c.c. | $[A_1]$. | $[B_1]$. | D, %. | log $[I_B]/[I_A]$. | log $[B_1]/[A_1]$. |
|---|---|---|---|---|---|---|
| | | Yellow form | | 18·7 | | |
| 2·50 | 1·50 | 0·00235 | 0·00390 | 25·1 | 0·671 | 0·220 |
| 3·00 | 1·50 | 0·00319 | 0·00347 | 27·1 | 0·546 | 0·037 |
| 5·00 | 1·50 | 0·00529 | 0·00240 | 35·9 | 0·196 | −0·343 |
| 6·00 | 1·50 | 0·00582 | 0·00208 | 38·0 | 0·135 | −0·447 |
| 8·00 | 1·50 | 0·00678 | 0·00164 | 45·1 | −0·043 | −0·616 |
| 10·00 | 1·50 | 0·00735 | 0·00135 | 53·5 | −0·224 | −0·745 |

*Salicylic acid.*

Mixtures : $A_1 = 0{\cdot}01043m$; $B_2 = 0{\cdot}01047m$.

| $A_1$, c.c. | $B_2$, c.c. | $[A_1]$. | $[B_1]$. | D, %. | log $[I_B]/[I_A]$. | log $[B_1]/[A_1]$. |
|---|---|---|---|---|---|---|
| . . . . | . . . . Yellow form | . . . . | . . . . | 23·0 | . . . . | . . . . |
| 2·30 | 2·00 | 0·000707 | 0·00487 | 42·0 | 0·164 | 0·838 |
| 2·40 | 2·00 | 0·000930 | 0·00476 | 50·0 | −0·060 | 0·706 |
| 2·50 | 2·00 | 0·001141 | 0·00465 | 58·0 | −0·222 | 0·610 |
| 2·60 | 2·00 | 0·001343 | 0·00455 | 67·0 | −0·456 | 0·530 |
| 3·00 | 2·00 | 0·002071 | 0·00419 | 80·0 | −0·745 | 0·306 |

*Monochloroacetic acid.*

Mixtures : $A_1 = 0{\cdot}01292m$; $B_2 = 0{\cdot}01153m$.

| | | | | | | |
|---|---|---|---|---|---|---|
| . . . . | . . . . Yellow form | . . . . | . . . . | 11·0 | . . . . | . . . . |
| 3·40 | 3·00 | 0·00146 | 0·00540 | 47·8 | −0·308 | 0·568 |
| 3·50 | 3·00 | 0·00164 | 0·00533 | 59·2 | −0·505 | 0·511 |
| 3·70 | 3·00 | 0·00197 | 0·00516 | 66·9 | −0·653 | 0·418 |
| 4·00 | 3·00 | 0·00244 | 0·00494 | 77·2 | −0·879 | 0·306 |

In the absence of association (or of some other effect) the expression $K = B_1I_A/A_1I_B$ would be constant for a given acid and indicator. That this expression is not constant is evident from the experimental data. For instance, in the case of salicylic acid the value of $K$ increases from 4·91 to 11·07 in the series taken. Again, no definite effect due to salt concentration on the value of $K$ could be found.

However, when allowance was made for association by the method suggested by LaMer and Downes, *i.e.*, when log $[I_B]/[I_A]$ was plotted against log $[B_1]/[A_1]$, straight-line graphs were obtained. The intercepts on the log $[B_1]/[A_1]$ axes were taken as a measure of the strengths of the acids relative to the indicator acid, 2 : 6-dinitrophenol.

When a comparison was made of the relative strengths in water and in chlorobenzene, the first six values in the table on p. 823 were obtained on a logarithmic scale. The dissociation constants of the acids in water are taken from Landolt–Börnstein " Tabellen," and those of the indicator from Kolthoff's " Säure-Basen-Indikatoren," Berlin, 1934. The constants are defined as

$$K_{\text{A.M.}} \text{ conventional} = c_{\text{base}}c_{\text{H}_2\text{O}}/c_{\text{acid}} \text{ for water}$$
$$K_{\text{A.F}^-} = c_{\text{base}}c_{\text{I}_\text{A}}/c_{\text{acid}}c_{\text{I}_\text{B}} \text{ for } c_{\text{I}_\text{B}}/c_{\text{I}_\text{A}} = 1 \text{ in chlorobenzene}$$
$$K_{\text{A.F}^-} = c_{\text{base}}c_{\text{I}_\text{A}}/c_{\text{acid}}c_{\text{I}_\text{B}} \text{ in water}$$

There is clearly a parallelism between the relative strengths of these acids in chlorobenzene and in water.

*Experiments with Bromophenol-blue.*—In water this indicator can exist in two forms, one blue and the other yellow; the $p_H$ of the colour change is 2·8—4·6. In certain other solvents it can exist in three or even four modifications: four forms are known in *m*-cresol (Brönsted, Delbanco, and Tovborg-Jensen, *loc. cit.*). When bromophenol-blue was dissolved in chlorobenzene the solution was practically colourless, and on addition of acids no colour was produced. On adding a weak base, such as *p*-toluidine, a yellow colour was produced, and if a strong base was added in sufficient quantity a green and eventually a blue colour was obtained. Thus, bromophenol-blue can exist in at least three forms in chlorobenzene. The three forms can be represented by the following alternative formulæ.

| I. | II. | | Net charge. |
|---|---|---|---|
| $\overset{+}{C}$ ($C_6H_2Br_2{\cdot}OH$)($C_6H_2Br_2{\cdot}OH$)($C_6H_4{\cdot}SO_3^-$) | C ($C_6H_2Br_2{\cdot}OH$)(=$C_6H_2Br_2{\cdot}OH^+$)($C_6H_4{\cdot}SO_3^-$) | Colourless | 0 |
| $\overset{+}{C}$ ($C_6H_2Br_2{\cdot}O^-$)($C_6H_2Br_2{\cdot}OH$)($C_6H_4{\cdot}SO_3^-$) | C ($C_6H_2Br_2{\cdot}OH$)(=$C_6H_2Br_2{:}O$)($C_6H_4{\cdot}SO_3^-$) | Yellow | −1 |
| $\overset{+}{C}$ ($C_6H_2Br_2{\cdot}O^-$)($C_6H_2Br_2{\cdot}O^-$)($C_6H_4{\cdot}SO_3^-$) | C ($C_6H_2Br_2{\cdot}O^-$)(=$C_6H_2Br_2{:}O$)($C_6H_4{\cdot}SO_3^-$) | Blue | −2 |

The colourless form is a strong acid. The blue form is not very soluble in chlorobenzene and is precipitated on standing, so it is not convenient to use the blue–yellow change for indicator

purposes. Since the colourless form is a strong acid, it is quite suitable for investigations with strong acids in chlorobenzene. The indicator equilibrium is:

$$\text{Colourless} \rightleftharpoons \text{Yellow} + H^+$$

The experimental procedure was almost identical with that employed in the case of 2 : 6-dinitrophenol. Allowance had to be made for the insolubility of the blue form of the indicator in chlorobenzene. A suitable concentration of indicator for measurements in the 1-cm. tube was produced by dissolving 0·05 g. in 25 c.c. of chlorobenzene and diluting the solution 50-fold. The indicator concentration was then approximately $6 \times 10^{-5}$*m*. As before, all the acid and base solutions were made up in this indicator solution. Readings were taken in the violet region. In order to produce the yellow colour, small quantities of *p*-toluidine were added to the indicator solution until a constant reading was obtained in the spectrophotometer. Since it was not practicable, owing to the insolubility of the blue form of the indicator, to make up solutions of the pure base, *iso*butylamine, in the indicator solution in chlorobenzene, the base was dissolved in a solution of the acid in the indicator solution. In this way two solutions were obtained: $A_1$, acid in indicator solution; M, acid + base in indicator solution.

*Monochloroacetic acid.* In order to determine if there was any variation in the value of $K$ at (1) constant salt concentration, (2) constant "total acid" concentration, the following experiments were carried out.

(1) In this series, three solutions, *viz.*, the pure indicator solution, an acid solution, and a solution of the base in acid solution, were used. The total volume and also the volume of M were maintained constant by adding pure solution of the indicator. When the salt concentration was maintained constant at 0·00193*m*, and the acid ($A_1$) concentration was decreased from 0·480 to 0·029*m*, the value of $K$ increased from 0·00229 to 0·00327. The variations in $K$ found in other experiments are thus not due to a salt effect alone. By plotting log $[I_B]/[I_A]$ against log [B]/[A], a straight line was obtained cutting the log [B]/[A] axis at −2·69.

(2) In order to maintain the total acid (free acid + salt) constant when the salt concentration was varied, two acid solutions and one solution of the base in one of the acid solutions were made up. The total volume was again kept constant, as well as the volume of the more concentrated acid solution. The acid concentration varied slightly (from 0·734 to 0·737*m*). The salt concentration was decreased from 0·00401 to 0·00120*m*. Meanwhile, $K$ increased gradually from 0·00161 to 0·00202. By plotting logarithms as before, the value −2·68 was obtained.

In a series in which the concentration both of the salt and of the total acid was varied, the following results were obtained.

*Monochloroacetic acid.*

Mixtures: $A_1$ = 0·1204*m*-acid; $M_1$ = 0·1204*m*-acid + 0·01055*m*-*iso*butylamine.

| $A_1$, c.c. | $M_1$, c.c. | [A]. | [B]. | D, %. | log $[I_B]/[I_A]$. | log [B]/[A]. |
|---|---|---|---|---|---|---|
| . . . | . . . | Yellow form | . . . | 24·7 | . . . | . . . |
| 2·0 | 2·0 | 0·1151 | 0·00528 | 26·3 | 1·332 | −1·338 |
| 3·0 | 2·0 | 0·1162 | 0·00422 | 26·6 | 1·255 | −1·440 |
| 5·0 | 2·0 | 0·1174 | 0·00301 | 28·2 | 0·985 | −1·591 |
| 8·2 | 2·0 | 0·1183 | 0·00211 | 29·6 | 0·872 | −1·749 |

*Dichloroacetic acid.*

Mixtures: $A_1$ = 0·0503*m*-acid; $M_1$ = 0·0503*m*-acid + 0·01055*m*-*iso*butylamine.

| | | | | | | |
|---|---|---|---|---|---|---|
| . . . | . . . | Yellow form | . . . | 5·9 | . . . | . . . |
| 1·00 | 2·00 | 0·0430 | 0·00733 | 15·9 | 0·261 | −0·770 |
| 1·60 | 2·00 | 0·0422 | 0·00611 | 21·5 | 0·070 | −0·857 |
| 2·00 | 2·00 | 0·0448 | 0·00550 | 22·9 | 0·030 | −0·910 |
| 2·50 | 2·00 | 0·0454 | 0·00489 | 26·6 | −0·061 | −0·967 |
| 3·00 | 2·00 | 0·0459 | 0·00440 | 30·3 | −0·141 | −1·014 |
| 5·00 | 2·00 | 0·0482 | 0·00314 | 41·1 | −0·342 | −1·177 |

*Trichloroacetic acid.* In order to see if the results could be reproduced under diverse conditions, several series of experiments were conducted with this acid, and good agreement was obtained when the intercepts on the *y* axes were compared as before. The description of one such experiment will suffice.

Mixtures: $A_1$ = 0·0186*m*-acid; $M_1$ = 0·0186*m*-acid + 0·01055*m*-*iso*butylamine.

| | | | | | | |
|---|---|---|---|---|---|---|
| . . . | . . . | Yellow form | . . . | 8·4 | . . . | . . . |
| 1·1 | 2·0 | 0·00406 | 0·00680 | 15·1 | 0·507 | 0·224 |
| 2·0 | 2·0 | 0·00558 | 0·00528 | 25·7 | 0·084 | −0·024 |
| 3·0 | 2·0 | 0·00664 | 0·00422 | 39·4 | −0·161 | −0·197 |
| 4·0 | 2·0 | 0·00734 | 0·00352 | 47·6 | −0·369 | −0·320 |
| [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] |

No value can be given for the strength of the colourless form of bromophenol-blue in water, since this form is immediately hydrolysed according to the scheme :

$$\text{Colourless} + H_2O = \text{Yellow} + H_3O^+$$

By comparison with colourless bromophenol-blue, the strengths on the logarithmic scale were :

| | | | |
|---|---|---|---|
| Monochloroacetic acid . . . | −2·69 | Trichloroacetic acid . . . | −0·09 |
| Dichloroacetic acid . . . | −0·94 | Bromophenol-blue (yellow form) . | 0·00 |

Since monochloroacetic acid also appears on the 2 : 6-dinitrophenol scale, the two series can be linked up and so one obtains the last three values in the following table.

| Acid. | Water. log $K_{A.M.}$ | Water. log $K_{A.F^-}$. | Chloro-benzene. log $K_{A.F^-}$. |
|---|---|---|---|
| Propionic ...... | $\bar{5}$·13 | −1·07 | −1·08 |
| Acetic ............ | $\bar{5}$·25 | −0·95 | −1·00 |
| Benzoic ......... | $\bar{5}$·81 | −0·39 | −0·58 |
| Dinitrophenol ... | $\bar{4}$·2 | 0·00 | 0·00 |
| Salicylic ......... | $\bar{3}$·02 | 0·82 | 0·74 |
| Monochloroacetic ... | $\bar{3}$·17 | 0·97 | 0·77 |
| Dichloroacetic ...... | $\bar{3}$·70 | 2·50 | 2·52 |
| Trichloroacetic ...... | — | — | 3·37 |
| Bromophenol-blue... | — | — | 3·46 |

Some of the above results were confirmed by similar experiments in which the Hilger–Nutting spectrophotometer was employed in the determination of the ratio of the two forms of the indicator. One example is quoted here.

*Monochloroacetic acid with* 2 : 6-*dinitrophenol.*

Mixtures : $A_1$, acid = 0·1022*m*, $B_2$, *iso*butylamine = 0·1039*m*. I = indicator in pure solvent.

| $A_1$, c.c. | $B_2$, c.c. | I, c.c. | [A]. | [B]. | log $[I_B]/[I_A]$. | log [B]/[A]. |
|---|---|---|---|---|---|---|
| 7·0 | 6·0 | 3·0 | 0·0056 | 0·0390 | 0·076 | 0·843 |
| 7·6 | 6·0 | 2·4 | 0·0095 | 0·0390 | −0·173 | 0·613 |
| 8·0 | 6·0 | 2·0 | 0·0120 | 0·0390 | −0·248 | 0·512 |
| 8·5 | 6·0 | 1·5 | 0·0151 | 0·0390 | −0·389 | 0·412 |
| 10·0 | 6·0 | 0·0 | 0·0248 | 0·0390 | −0·555 | 0·196 |

When the logarithms are plotted as before, one finds the constant for this acid to be 0·79, which is in good agreement with the value obtained by use of the other apparatus.

All the acids are not associated to the same extent relative to the indicator, and for an individual acid the slopes are different on the curves drawn, but the point of intersection of the vertical axis was practically the same for any one acid. This would indicate that the figures given fairly accurately represent the relative strengths of acids in chlorobenzene, and the close parallelism between these values and those in water indicates, further, that the activity coefficients of the acids undergo almost parallel changes in passing from water to benzene or chlorobenzene.

It is shown that trichloroacetic acid and bromophenol-blue, both just " strong " acids in water, are about ten times as strong as dichloroacetic acid in chlorobenzene.

Thanks are due to Professor J. N. Brönsted, at whose suggestion this work was started and under whose guidance it was continued, first in his laboratory in Copenhagen and later in Cardiff. I am also indebted to Professor T. Graham Brown, F.R.S., and Dr. John Pryde for providing me with laboratory facilities.

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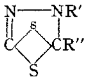
The Institute of Physiology, Newport Road, Cardiff. [*Received, July 5th,* 1937.]

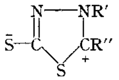
## 158. *The Constitution and Isomerism of Certain Triazole Derivatives of the Nitron Type in the Light of the Bredt Rule and the Theory of Resonance.**

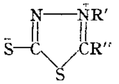
By Alexander Schönberg.

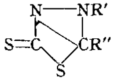
The generally accepted formula of certain di- and tri-azole derivatives is not in accordance with the laws of stereochemistry. These substances have hitherto been regarded as containing condensed ring systems, but now they are regarded as "Zwitterione." In certain cases (compare X) the old formula mnst be replaced by *two* different formulæ [compare VIII*a* and VIII*b* (R = Ph, R′ = $CH_2Ph$)] representing two isomerides. In this, as in other cases, the existence of two isomerides has been established, a phenomenon which could not be explained by the classical formula.

The chemical properties of certain *endo*thiodihydrothiodiazoles have been thoroughly investigated, especially by Busch and his co-workers (cf. *J. pr. Chem.*, 1903, **67**, 201—264, where other references are also given), and they are generally regarded as having the structure


(I.)

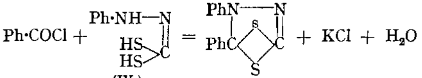

(II.)

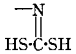

(III.)


(III*a*.)

(I). This formula, however, does not conform to Bredt's rule (*Annalen*, 1924, **437**, 1) that, in the simpler polycyclic compounds, as in five- and six-membered rings, a double bond is never attached to the carbon atoms at the end of the bridge: recognition of this rule led to the revision of the formula of santene *inter alia*.

Notwithstanding this, formula (I) might be valid if it represented labile compounds, but actually those of this type are very stable to heat; *e.g.*, (I; R′ = R″ = Ph) has m. p. 224°. The reaction mechanism (A) given by Busch and his co-workers for the formation of these compounds cannot be used as support for the polycyclic formula advanced by them, since in (IV) the valencies are distorted; *i.e.*, the two univalent groups are situated on one side of a double bond, whereas in reality they are situated one on each side as in (IV*a*).

(A.) 
(IV.)

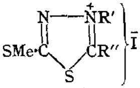

(IV*a*.)

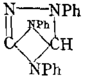
(i) The suggestion is now advanced that these *endo*thiodihydrothiodiazoles should be regarded as compounds with intramolecular ionogenic bonds (cf. II) and the modern views of resonance are applied in this connexion. These compounds are accordingly to be regarded as resonance hybrids between (II) and (III) and the other possible formulæ according to the theory of resonance. The new formulation takes Bredt's rule into account and is in excellent agreement with the chemical properties of this class of compound—*e.g.*, (V; R′ = R″ = Ph) is formed in a few minutes by boiling (I) with an alcoholic solution of methyl iodide (Busch, Kamphausen, and Schneider, *J. pr. Chem.*, 1903, **67**, 222); on the older idea this involves a breaking of the C–S–C bond which, under such conditions, is most improbable, but if (I) is replaced by (II) or (III) the formation of (V) is easily understandable.

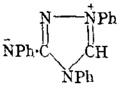
(ii) Considerations similar to those given above lead to rejection of the classical formulæ for the *endo*iminotriazolines, also known as *endo*iminodihydrotriazoles (cf. Wittig,

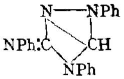
* See Pauling and Sherman, *J. Chem. Physics*, 1933, **1**, 606; Arndt and Eistert, *Z. physikal. Chem.*, 1935, *B*, **31**, 125; Sidgwick, J., 1937, 694; General Discussion on Dipole Moments, *Trans. Faraday Soc.*, 1934, **30**, 677, which gives other references. (Added in proof) See also Ingold, *Nature*, 1938, **141**, 314; Kenner, *ibid.*, p. 786.

" Stereochemie," p. 179, in connexion with the strain properties in *N*-ring systems and the Bredt rule). It is therefore now proposed to use the betaine structure (VII) instead of (VI) for nitron, which is a pale yellow compound of high m. p. (231°). The resonance theory may also be applied to (VII).

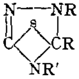

(V.)

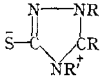

(VI.)

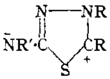

(VII.)

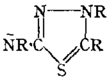

(VII*a*.)

(iii) The application of the above ideas to the *endo*thio- and *endo*oxy-triazolines (known also as *endo*thio- and *endo*oxy-dihydrotriazoles respectively) leads to the possibility of new isomerides, for *each* of the classical formulæ must be replaced by *two betaine* formulæ. For instance, (VIII) has hitherto been used for the two isomers (VIII*a*) and (VIII*b*), but now for compounds of this series it will be necessary to determine whether they are *S*-(VIII*b*) or *N*-*cyclo*-compounds (VIII*a*): each formula represents a distinct compound and to each isomer the rules of mesomerism are applicable, so that (VIII*b*) may be replaced by (VIII*c*). Similar considerations apply to the oxygen analogues (cf. IX).


(VIII.)


(VIII*a*.)

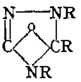

(VIII*b*.)

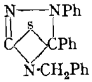

(VIII*c*.)

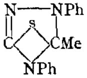
The puzzling isomeric properties of the *endo*thiotriazolines are explained by the above considerations and it is now no longer necessary, as was formerly the case in a number of instances, to represent by *one* formula *two* compounds with quite different m. p.'s. For example, the compound previously represented by (X) occurs in pale yellow needles, m. p. above 250° (mostly at 255—256°), and decomposes on standing into a crystalline powder which, recrystallised from chloroform-alcohol, has m. p. 236° (Busch, Kamphausen, and Schneider, *loc. cit.*, pp. 218, 228). Further, the disagreement between Busch and Renner (*Ber.*, 1934, **67**, 386) on the one hand and McKee (J., 1915, **107**, 1135) on the other is explained, for our conception requires that the compound previously formulated as (XI) should occur in two forms (cf. VIII*a* and VIII*b*). Since the form of m. p. 256° is readily converted into that of m. p. 233°, it seems impossible to establish by chemical means which of the isomers belongs to the *S*-series and which to the *N*-series.

(iv) It still remains to be decided whether for the dihydrotriazole derivatives mentioned in this paper formulæ containing three-membered rings should be assigned instead of the betaine formulæ; *e.g.*, whether nitron should be formulated as (VII*a*). This structure is untenable, however, for nitron is " extraordinarily stable to hydrochloric acid at higher temperatures " (Busch, *J. pr. Chem.*, 1906, **74**, 535), whereas a compound of formula (VII*a*) would certainly under such conditions yield aniline.

Similarly, (I) cannot be replaced by (III*a*) instead of by (II), for these compounds are very stable to mercuric oxide even when they are in boiling benzene solution, and such stability is quite incompatible with the presence of the >C=S group which (III*a*) demands (Busch, *loc. cit.*, p. 204; cf. also Schönberg, van Vargha, and Paul, *Annalen*, 1930, **483**, 109).


(IX.)


(X.)


(XI.)

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# 159. *Boiling Point and Chemical Constitution. Part I. An Additive Function of Molecular Weight and Boiling Point.*

By V. C. E. BURNOP.

The empirical quantity $M \log_{10}T + 8{\cdot}0\sqrt{M}$, denoted by (*b*), where *M* is the molecular weight and *T* the boiling point in degrees absolute, is shown to be additive. By examining the values of (*b*) for a number of compounds, the contributions to (*b*) of the separate atoms and structures within the molecule are found.

VARIOUS relations have been suggested between the boiling points of the members of homologous series and their molecular weights. Kopp (*Annalen*, 1842, **41**, 79, 86, 169) thought that the difference in boiling point between successive members of homologous series was always 19°, but Schorlemmer (*ibid.*, 1872, **161**, 281; 1878, **170**, 150; *Ber.*, 1871, **4**, 359, 564; 1874, **7**, 1131) showed that this rule was incorrect and that the $CH_2$ difference falls off continuously as molecular weight increases. Young (*Phil. Mag.*, 1905, **9**, 1) found that the difference *D* between the boiling point *T* of any compound and that of the next higher homologue is given by $D = 144{\cdot}86/T^{0{\cdot}0148\sqrt{T}}$. Walker (J., 1894, **65**, 193) put forward the expression $T = aM^b$, where *T* is the absolute boiling point, *M* the molecular weight, and *a* and *b* constants for a given homologous series. Boggio-Lera (*Gazzetta*, 1899, **29**, i, 441) modified this to the form $T = a\sqrt{M} + b$. Ramage used $T = aM\,(1 - 2^{-n})^{\frac{1}{2}}$, where *n* is the number of carbon atoms in the molecule. These expressions were applied to non-associated liquids. They relate boiling point and molecular weight, but are not otherwise concerned with molecular structure.

It is proposed to show that the expression $M \log_{10}T + 8{\cdot}0\sqrt{M}$, where *T* is the absolute boiling point at atmospheric pressure and *M* the molecular weight, is additive. The value of this function for any compound will be denoted by (*b*), this symbol also being used for the atomic and structural values.

From the values of (*b*) calculated for various homologous series, the following atomic and structural values have been obtained:

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| C | 23·2 | F | 68 | O | 51·0 | Br | 255 | Double bond | 16·1 |
| H | 10·9 | Cl | 121·0 | N | 39·7 | I | 398 | Triple bond | 33·0 |
| | | | | | | | | Six-membered ring | 17·6 |

Values of (*b*) derived from the observed boiling point are compared below with those calculated according to the figures just given.

*Normal Paraffins*, $C_nH_{2n+2}$; $(b) = 21{\cdot}8 + 45{\cdot}03n$.

| *n*. | (*b*), obs. | (*b*), calc. | *n*. | (*b*), obs. | (*b*), calc. | *n*. | (*b*), obs. | (*b*), calc. |
|---|---|---|---|---|---|---|---|---|
| 1 | 64·8 | 66·8 | 7 | 337·3 | 337·0 | 13 | 606·8 | 607·2 |
| 2 | 112·0 | 111·9 | 8 | 382·1 | 382·0 | 14 | 652·1 | 652·2 |
| 3 | 156·9 | 156·9 | 9 | 427·1 | 427·1 | 15 | 696·9 | 697·3 |
| 4 | 202·3 | 201·9 | 10 | 472·0 | 472·1 | 16 | 742·3 | 742·3 |
| 5 | 247·3 | 247·0 | 11 | 517·0 | 517·1 | 17 | 787·4 | 787·3 |
| 6 | 292·1 | 292·0 | 12 | 561·8 | 562·2 | 18 | 832·3 | 832·4 |

A branched-chain compound has a lower boiling point than the corresponding straight-chain compound:

*Pentanes.*

| | *T*. | (*b*), obs. | Decrease. |
|---|---|---|---|
| $CH_2Me{\cdot}CH_2{\cdot}CH_2Me$ | 309° | 247·3 | — |
| $CHMe_2{\cdot}CH_2Me$ | 301 | 246·4 | 0·9 |
| $CMe_4$ | 283 | 244·6 | 2·7 |

*Hexanes.*

| | *T*. | (*b*), obs. | Decrease. |
|---|---|---|---|
| $CH_2Me{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Me$ | 342° | 292·1 | — |
| $CHMe(CH_2Me)_2$ | 337 | 291·8 | 0·3 |
| $CH_2Me{\cdot}CH_2{\cdot}CHMe_2$ | 335 | 291·5 | 0·6 |
| $CHMe_2{\cdot}CHMe_2$ | 331 | 291·0 | 1·1 |
| $CH_2Me{\cdot}CMe_3$ | 322 | 290·0 | 2·1 |

Also, a β-methyl group causes a decrease in (*b*) of about 0·9.

| | (*b*), obs. *n*. | (*b*), obs. *iso*. | Diff. |
|---|---|---|---|
| Butane | 202·3 | 201·4 | 0·9 |
| Pentane | 247·3 | 246·4 | 0·9 |
| Hexane | 292·1 | 291·5 | 0·6 |
| Heptane | 337·3 | 336·2 | 1·1 |
| Octane | 382·1 | 381·1 | 1·0 |

*Unsaturated Hydrocarbons.*—For the olefins, the calculated values of (*b*) agree very closely with those derived from observation. Among isomers, that with the double bond in the αβ-position has the lowest b. p. For those compounds in the table the mean values are: for an αβ-double bond, 16·0; for a βγ-double bond, 16·4; for a γδ-double bond, 16·3. A similar feature is noticed with the acetylenes: for an αβ-triple bond, 32·5; for a βγ-triple bond, 34·0. With the diolefins, the b. p. decreases as the number of carbon atoms between the double bond increases:

| | | | |
|---|---|---|---|
| No. of C atoms between bonds | 1 | 2 | 3 |
| (*b*) for the double bond | 16·7 | 16·4 | 15·7 |

| Olefin. | (*b*), obs. | (*b*), calc. |
|---|---|---|
| $CH_2:CH_2$ | 104·6 | 106·1 |
| $CH_2:CHMe$ | 150·8 | 151·1 |
| $CH_2:CH{\cdot}CH_2Me$ | 196·1 | 196·1 |
| $CHMe:CHMe$ | 196·8 | ,, |
| $CH_2:CH{\cdot}[CH_2]_2{\cdot}CH_3$ | 241·9 | 241·1 |
| $CHMe:CH{\cdot}CH_2Me$ | 241·6 | ,, |
| $CH_2:CH{\cdot}[CH_2]_3{\cdot}CH_3$ | 285·8 | 286·1 |
| $CHMe:CH{\cdot}[CH_2]_2{\cdot}CH_3$ | 286·2 | ,, |
| $CH_2Me{\cdot}CH:CH{\cdot}CH_2Me$ | 286·5 | 286·1 |
| $CH_2:CH{\cdot}[CH_2]_4{\cdot}CH_3$ | 330·9 | 331·1 |
| $CHMe:CH{\cdot}[CH_2]_3{\cdot}CH_3$ | 331·2 | ,, |
| $CH_2Me{\cdot}CH:CH{\cdot}[CH_2]_2{\cdot}CH_3$ | 331·1 | ,, |
| $CH_2:CH{\cdot}[CH_2]_5{\cdot}CH_3$ | 375·8 | 376·1 |
| $CH_2:CH{\cdot}[CH_2]_6{\cdot}CH_3$ | 421·0 | 421·1 |
| $CH_2:CH{\cdot}[CH_2]_7{\cdot}CH_3$ | 465·7 | 466·1 |

| Diolefin. | (*b*), obs. | (*b*), calc. |
|---|---|---|
| $CH_2:C:CH_2$ | 146·1 | 145·4 |
| $CH_2:C:CHMe$ | 192·0 | 190·4 |
| $CH_2:CH{\cdot}CH:CH_2$ | 190·2 | ,, |
| $CH_2:CH{\cdot}CH:CHMe$ | 236·0 | 235·4 |
| $CH_2:C:CH{\cdot}CH_2Me$ | 236·3 | ,, |
| $CH_2:CH{\cdot}CH_2{\cdot}CH:CH_2$ | 234·5 | 235·4 |
| $CHMe:C:CHMe$ | 236·6 | ,, |
| $CH_2:CH{\cdot}[CH_2]_2{\cdot}CH:CH_2$ | 279·3 | 280·4 |
| $CHMe:CH{\cdot}CH:CHMe$ | 281·6 | ,, |

| Acetylene. | (*b*), obs. | (*b*), calc. |
|---|---|---|
| $CH:CH$ | 99·7 | 101·2 |
| $CH:CMe$ | 146·6 | 146·2 |
| $CH:C{\cdot}CH_2Me$ | 191·9 | 191·2 |
| $CMe:CMe$ | 192·9 | ,, |
| $CH:C{\cdot}CH_2{\cdot}CH_2Me$ | 235·8 | 236·2 |
| $CMe:C{\cdot}CH_2Me$ | 237·3 | ,, |
| $CH:C{\cdot}[CH_2]_3{\cdot}CH_3$ | 280·5 | 281·2 |
| $CMe:C{\cdot}[CH_2]_2{\cdot}CH_3$ | 281·8 | ,, |
| $CH:C{\cdot}[CH_2]_4{\cdot}CH_3$ | 325·4 | 326·2 |
| $CMe:C{\cdot}[CH_2]_3{\cdot}CH_3$ | 326·8 | ,, |
| $CH:C{\cdot}[CH_2]_5{\cdot}CH_3$ | 370·2 | 371·2 |
| $CH:C{\cdot}[CH_2]_6{\cdot}CH_3$ | 415·1 | 416·2 |

cyclo*Paraffins.*—The presence of a ring causes an increase in (*b*) of the same order as that due to a double bond.

| Hydrocarbon. | (*b*), obs. | (*b*) for ring. |
|---|---|---|
| *cyclo*Propane | 151·0 | 16·0 |
| *cyclo*Butane | 197·7 | 17·7 |
| *cyclo*Pentane | 242·8 | 17·8 |
| *cyclo*Hexane | 287·6 | 17·6 |
| Methyl*cyclo*hexane | 332·3 | 17·3 |
| *cyclo*Heptane | 333·4 | 18·4 |
| *cyclo*Octane | 378·5 | 18·5 |
| *cyclo*Nonane | 423·7 | 18·7 |

*Aromatic Hydrocarbons.*—The value of (*b*) calculated for the Kekulé formula for benzene agrees well with the value derived from the b. p. Thus: $C_6$ = 139·2, $H_6$ = 65·4, three double bonds = 48·3, six-membered ring = 17·6, giving (*b*), calc. = 270·5. The observed value is 269·6.

| Hydrocarbon. | (*b*), obs. | (*b*), calc. |
|---|---|---|
| Benzene | 269·6 | 270·5 |
| Toluene | 314·3 | 315·5 |
| Ethylbenzene | 359·3 | 360·5 |
| Propylbenzene | 404·0 | 405·5 |
| Butylbenzene | 448·9 | 450·5 |
| Amylbenzene | 493·8 | 495·5 |

The transition from *cyclo*hexane to benzene is shown in the following table:

| | (*b*), obs. | (*b*), calc. |
|---|---|---|
| *cyclo*Hexane | 287·6 | (287·6) |
| *cyclo*Hexene | 282·0 | 281·9 |
| *cyclo*Hexa-1 : 3-diene | 275·5 | 276·2 |
| *cyclo*Hexa-1 : 4-diene | 276·1 | 276·2 |
| Benzene | 269·6 | 270·5 |

Where two rings are fused together, each ring exerts its separate value of (*b*), as in the following table:

| Hydrocarbon. | Rings. | Double bonds. | (*b*), obs. | (*b*), calc. |
|---|---|---|---|---|
| Naphthalene, $C_{10}H_8$ | 2 | 5 | 435·2 | 434·9 |
| Tetrahydronaphthalene, $C_{10}H_{12}$ | 2 | 3 | 462·3 | 463·4 |
| Decahydronaphthalene, $C_{10}H_{18}$ | 2 | 0 | 451·9 | 454·8 |
| Anthracene, $C_{14}H_{10}$ | 3 | 7 | 604·8 | 599·3 |

*The Halogens.*—The following figures are obtained for the halogens at their b. p.'s together with those for the hydrogen halides.

| Halogen. | (*b*), obs. | (*b*), calc. | Hydrogen halide. | (*b*), obs. | (*b*), calc. |
|---|---|---|---|---|---|
| $F_2$ | 141·8 | 136 | HCl | 131·5 | 131·9 |
| $Cl_2$ | 236·2 | 242 | HBr | 254·2 | 266 |
| $Br_2$ | 504·2 | 510 | HI | 394·5 | 409 |
| $I_2$ | 802·3 | 796 | | | |

*Alkyl Chlorides,* $C_nH_{2n+1}Cl$.—Values for the α- and β-chloro-*n*-paraffins are here compared with the values calculated from a mean figure for Cl. The b. p.'s of the β-chloro paraffins are lower than those of the α-compounds, causing a difference of about 1·5 in (*b*) between isomers in the two series.

| *n*. | (*b*), obs., α-chloro. | (*b*), obs., β-chloro. | (*b*), calc. | *n*. | (*b*), obs., α-chloro. | (*b*), obs., β-chloro. | (*b*), calc. |
|---|---|---|---|---|---|---|---|
| 1 | 178·0 | — | 176·9 | 5 | 357·5 | 356·1 | 356·9 |
| 2 | 222·7 | — | 221·9 | 6 | 402·2 | 401·0 | 401·9 |
| 3 | 267·7 | 266·4 | 266·9 | 7 | 447·6 | 446·0 | 446·9 |
| 4 | 312·4 | 311·3 | 311·9 | 8 | 493·0 | 491·1 | 491·9 |

n-*Alkyl bromides,* $C_nH_{2n+1}Br$.

| *n*. | (*b*), obs. | (*b*), calc. | *n*. | (*b*), obs. | (*b*), calc. |
|---|---|---|---|---|---|
| 1 | 310·5 | 311 | 5 | 491·5 | 491 |
| 2 | 355·1 | 356 | 6 | 537·0 | 536 |
| 3 | 400·7 | 401 | 7 | 582·2 | 581 |
| 4 | 446·2 | 446 | 8 | 628·1 | 626 |

n-*Alkyl iodides,* $C_nH_{2n+1}I$.

| *n*. | (*b*), obs. | (*b*), calc. | *n*. | (*b*), obs. | (*b*), calc. |
|---|---|---|---|---|---|
| 1 | 449·9 | 454 | 5 | 634·0 | 634 |
| 2 | 494·8 | 499 | 6 | 679·2 | 679 |
| 3 | 541·8 | 544 | 7 | 725·7 | 724 |
| 4 | 588·2 | 589 | 8 | 771·7 | 769 |

*Halogenobenzenes.*

| | (*b*), obs. | (*b*), calc. | | (*b*), obs. | (*b*), calc. |
|---|---|---|---|---|---|
| Fluorobenzene | 323·8 | 327·6 | Bromobenzene | 516·1 | 514·6 |
| Chlorobenzene | 378·0 | 380·6 | Iodobenzene | 657·9 | 657·6 |

*Ethers and Esters.*—These yield good results, (*b*), calc. being very near (*b*), obs. Among isomers that with the lowest b. p. is that in which the two groups R and R′ are the same, or differ only by $CH_2$. In the tables all the alkyl groups are normal. The double bond in the carbonyl group of the esters has the same value of (*b*) as in the olefins.

| Ether. | (*b*), obs. | (*b*), calc. | Ether. | (*b*), obs. | (*b*), calc. | Ether. | (*b*), obs. | (*b*), calc. |
|---|---|---|---|---|---|---|---|---|
| Dimethyl | 164·7 | 162·8 | Methyl heptyl | 433·0 | 432·8 | Dioctyl | 791·0 | 792·8 |
| Methyl ethyl | 209·1 | 207·8 | Ethyl hexyl | 431·2 | ,, | Benzyl ethyl | 455·4 | 455·2 |
| Diethyl | 253·3 | 252·8 | Dibutyl | 431·8 | ,, | Phenyl methyl | 367·6 | 365·2 |
| Methyl butyl | 298·5 | 297·8 | Ethyl heptyl | 477·1 | 477·8 | Phenyl ethyl | 412·4 | 410·2 |
| Methyl amyl | 341·8 | 342·8 | Ethyl octyl | 521·3 | 522·8 | Phenyl propyl | 456·1 | 458·2 |
| Ethyl butyl | 342·2 | ,, | Diamyl | 522·4 | ,, | Phenyl hexyl | 590·5 | 590·2 |
| Dipropyl | 342·1 | ,, | Dihexyl | 612·1 | 612·8 | Diphenyl | 567·8 | 570·8 |
| Ethyl amyl | 387·4 | 387·8 | Diheptyl | 701·1 | 702·8 | | | |

| Ester. | (*b*), obs. | (*b*), calc. | Ester. | (*b*), obs. | (*b*), calc. | Ester. | (*b*), obs. | (*b*), calc. |
|---|---|---|---|---|---|---|---|---|
| Methyl formate | 211·1 | 208·1 | Methyl valerate | 388·5 | 388·1 | Amyl acetate | 432·6 | 433·1 |
| Methyl acetate | 255·5 | 253·1 | Ethyl butyrate | 387·7 | ,, | Hexyl formate | 433·4 | ,, |
| Ethyl formate | 255·2 | ,, | Propyl propionate | 387·9 | ,, | Methyl heptoate | 477·7 | 478·1 |
| Methyl propionate | 299·4 | 298·1 | Butyl acetate | 388·4 | ,, | Ethyl hexoate | 477·0 | ,, |
| Ethyl acetate | 299·2 | ,, | Amyl formate | 388·9 | ,, | Propyl valerate | 477·2 | ,, |
| Propyl formate | 299·5 | ,, | Methyl hexoate | 432·8 | 433·1 | Butyl butyrate | 477·0 | ,, |
| Methyl butyrate | 343·6 | 343·1 | Ethyl valerate | 432·2 | ,, | Amyl propionate | 476·8 | ,, |
| Ethyl propionate | 343·2 | ,, | Propyl butyrate | 431·8 | ,, | Hexyl acetate | 477·5 | ,, |
| Propyl acetate | 343·5 | ,, | Butyl propionate | 432·2 | ,, | Heptyl formate | 478·3 | ,, |
| Butyl formate | 344·1 | ,, | | | | | | |

*Aromatic esters.*

| | (*b*), obs. | (*b*), calc. | | (*b*), obs. | (*b*), calc. |
|---|---|---|---|---|---|
| Methyl benzoate | 457·2 | 455·5 | Benzyl acetate | 501·4 | 500·5 |
| Ethyl benzoate | 501·1 | 500·5 | Phenyl benzoate | 661·2 | 660·5 |

*Ketones.*—With the value of (*b*) already found for the double bond from the olefins, the values of (*b*), obs. for the aliphatic ketones are 2·9 units lower than the calculated. The

differences amount to only 0·5—1·5% of the whole, but the constancy is remarkable. On the other hand, the aromatic ketones have values of (*b*) higher than the calculated.

| Ketone. | (*b*), obs. | (*b*), calc. | Diff. |
|---|---|---|---|
| Dimethyl | 199·2 | 202·1 | 2·9 |
| Methyl ethyl | 244·3 | 247·1 | 2·8 |
| „ propyl | 289·5 | 292·1 | 2·6 |
| „ butyl | 334·4 | 337·1 | 2·7 |
| „ amyl | 379·6 | 382·1 | 2·5 |
| „ hexyl | 424·8 | 427·1 | 2·3 |
| „ heptyl | 469·0 | 472·1 | 3·1 |
| „ octyl | 514·8 | 517·1 | 2·3 |
| „ nonyl | 559·5 | 562·1 | 2·6 |
| Diethyl | 289·2 | 292·1 | 2·9 |
| Ethyl propyl | 334·1 | 337·1 | 3·0 |
| „ butyl | 379·5 | 382·1 | 2·6 |
| „ amyl | 424·1 | 427·1 | 3·0 |

| Ketone. | (*b*), obs. | (*b*), calc. | Diff. |
|---|---|---|---|
| Ethyl hexyl | 469·5 | 472·1 | 2·6 |
| „ heptyl | 514·5 | 517·1 | 2·6 |
| „ octyl | 558·7 | 562·1 | 3·4 |
| Dipropyl | 378·9 | 387·1 | 3·2 |
| Dibutyl | 468·8 | 472·1 | 3·3 |
| Diamyl | 559·2 | 562·1 | 2·9 |
| Phenyl methyl | 408·0 | 405·8 | 2·2 |
| „ ethyl | 453·6 | 450·8 | 2·8 |
| Benzyl methyl | 453·5 | 450·8 | 2·7 |
| „ ethyl | 497·5 | 495·8 | 1·7 |
| Diphenyl | 610·9 | 609·5 | 1·4 |
| Dibenzyl | 700·2 | 699·5 | 0·7 |

*Amines.*—The value of (*b*) for nitrogen was obtained from the differences between the aromatic compounds and the corresponding heterocyclic compounds in which the CH group is replaced by the nitrogen atom:

| Heterocyclic. | (*b*). | Aromatic. | (*b*). | Diff. | (*b*) for N. |
|---|---|---|---|---|---|
| Pyridine | 275·7 | Benzene | 269·6 | 6·1 | 40·2 |
| Quinoline | 440·3 | Naphthalene | 435·2 | 5·1 | 39·2 |
| Piperidine | 293·1 | *cyclo*Hexane | 287·6 | 5·5 | 39·6 |

The mean value of 39·7 leads to good agreement between the values of (*b*) observed and calculated for the amines. Usually the former is 1—2 units high but this is possibly explained by association.

n-*Alkylamines*, $C_nH_{2n+1}\cdot NH_2$.

| *n*. | (*b*), obs. | (*b*), calc. | *n*. | (*b*), obs. | (*b*), calc. | *n*. | (*b*), obs. | (*b*), calc. |
|---|---|---|---|---|---|---|---|---|
| 1 | 119·7 | 117·4 | 6 | 343·7 | 342·4 | 10 | 523·4 | 522·4 |
| 2 | 163·7 | 162·4 | 7 | 388·8 | 387·4 | 11 | 567·7 | 567·4 |
| 3 | 209·9 | 207·4 | 8 | 433·8 | 432·4 | 12 | 612·5 | 612·4 |
| 4 | 254·3 | 252·4 | 9 | 478·7 | 477·4 | 13 | 657·0 | 657·4 |
| 5 | 298·9 | 297·4 | | | | | | |

*Other amines.*

| | (*b*), obs. | (*b*), calc. | | (*b*), obs. | (*b*), calc. | | (*b*), obs. | (*b*), calc. |
|---|---|---|---|---|---|---|---|---|
| $NH_3$ | 73·4 | 72·4 | $NEt_3$ | 339·0 | 342·4 | NHMePh | 368·8 | 366·1 |
| $NH_2\cdot NH_2$ | 128·2 | 123·0 | $NH_2Ph$ | 324·8 | 321·1 | $NMe_2Ph$ | 411·0 | 411·1 |
| $NHMe_2$ | 164·0 | 163·7 | $NHPh_2$ | 570·8 | 569·8 | NHEtPh | 411·6 | 411·1 |
| $NMe_3$ | 206·8 | 207·4 | $NPh_3$ | 813·0 | 815·9 | $NEt_2Ph$ | 498·7 | 501·1 |
| $NHEt_2$ | 252·4 | 252·4 | | | | | | |

The compounds dealt with in this paper (hydrocarbons, alkyl halides, ethers, esters, ketones, and amines) show clearly that the function (*b*) is additive. Associated compounds, such as the alcohols and the acids, have values of (*b*) higher than calculated, and it is proposed to treat them separately in a further paper.

IMPERIAL COLLEGE, LONDON, S.W. 7. [*Received, April 28th*, 1938.]

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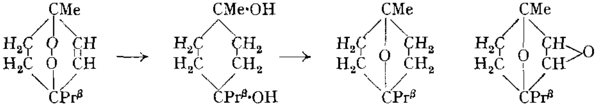
## 160. *Chenopodium Oil. Part III. Ascaridole.*

By HUMPHREY PAGET.

Ascaridole, the active principle of chenopodium oil, is an unsaturated terpene peroxide. It is decomposed explosively by heat or by treatment with concentrated mineral acids. Difficulty has been experienced in estimating its amount in chenopodium oil, and the only chemical methods described, by reduction with acid solutions of titanous chloride or of potassium iodide, involve the use of empirical factors. This may be due either to ascaridole being in reality a mixture or to the complexity of its reaction with these reducing agents. Ascaridole has now been

obtained crystalline by cooling to about −20°, but purification in this way has given no evidence that it is a mixture. Reduction by titanous chloride leads to a complex mixture of products. Rupture of the peroxide bridge with evolution of propane and formation of *p*-cresol takes place to the extent of 33%; isomerisation and condensation also occur. *Dihydroascaridole*, a saturated peroxide formed by hydrogenation of ascaridole with one mol. of hydrogen, is reduced by titanous chloride with production, in 90% yield, of propane and 1-*methyl*cyclo*hexan*-1-*ol* 3 : 4-*oxide*. The latter substance is oxidised by chromic acid to the lactone of β-hydroxy-β-methyladipic acid.

ASCARIDOLE, the anthelmintic constituent of chenopodium oil, was given the formula of an unsaturated 1 : 4-peroxide (I) by Wallach (*Annalen*, 1912, **392**, 59) from consideration of the products of hydrogenation in presence of palladium. He showed that it absorbed two mols. of hydrogen, yielding *cis*-1 : 4-terpin (II), which on dehydration by oxalic acid solution gave $\Delta^1$-*p*-menthen-4-ol and 1 : 4-cineole (III).



(I.) (II.) (III.) (IV.)

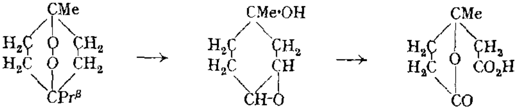
Although ascaridole absorbs the calculated quantity of hydrogen for conversion into 1 : 4-terpin, it does not react in a quantitative manner with reducing agents such as titanous chloride (Paget, *Analyst*, 1926, **51**, 170) or potassium iodide in hydrochloric and acetic acids (Cocking and Hymas, *Analyst*, 1930, **55**, 180), and methods of estimation based on the use of these reagents require the application of an empirical factor. On the basis of the addition of four atoms of hydrogen, 34·7% of the calculated amount of reducing agent is utilised in the case of titanous chloride, and 63·3% in the case of the second reagent by the process described in the British Pharmacopœia (1932). These facts suggest either that ascaridole is a mixture of two substances which cannot be separated by distillation or that attack by these somewhat strongly acid reagents on the peroxide bridge involves a number of reactions leading to a complex mixture of products.

Ascaridole is not easily purified by distillation, since it is isomerised by heat to a more stable dioxide (IV), the boiling point of which lies near that of ascaridole itself. By cooling in solid carbon dioxide it has now been obtained crystalline; it separates from a number of solvents, such as alcohol, light petroleum, *iso*propyl ether or the terpene fraction of chenopodium oil, but repeated crystallisation in this way has not resulted in a separation.

The principal products of reduction of ascaridole by an acid solution of titanous chloride, which have been identified, are propane and *p*-cresol, each in about 33% yield. The evolution of a combustible gas has already been observed by Nelson (*J. Amer. Chem. Soc.*, 1911, **33**, 1407) during reduction by ferrous sulphate, and by Wallach (*loc. cit.*) during isomerisation to the dioxide by heat. No intermediate products of reduction have been identified and if they were formed they would undoubtedly be rapidly decomposed under the conditions of the reaction, since all the products of catalytic hydrogenation are highly unstable in presence of mineral acids. A considerable amount of an uncrystallisable syrup is obtained, which contains chlorine and cannot be distilled without decomposition. This has yielded very small amounts of crystalline acylated products, an unsaturated *glycol*, $C_{10}H_{18}O_2$, m. p. 84°, and a *substance*, $C_{10}H_{19}O_3Cl$, m. p. 191°, which has the composition of a chlorotrihydroxymenthane. The identification of ascaridole-α-glycol as its *mono*- and *di-nitrobenzoates* indicates that some isomerisation to the dioxide has taken place.

By partial hydrogenation of ascaridole with one mol. of hydrogen, using a palladised charcoal catalyst, Richter and Presting (*Ber.*, 1931, **64**, 878) obtained $\Delta^8$-*p*-menthene-1 : 4-diol, in which the peroxide structure alone is reduced and which does not react with titanous chloride. This is not, however, the sole product, and an oil has been isolated which is no doubt *dihydroascaridole* (V), formed by preferential hydrogenation of the

ethylenic linkage, leaving the peroxide bridge intact. When partial hydrogenation is carried out in presence of platinum oxide instead of palladium, dihydroascaridole appears to be the only product. It contains no hydroxyl group, but, like the menthenediol, on further hydrogenation yields *cis*-1 : 4-terpin. On reduction by titanous chloride it gives rise to propane in about 90% yield and a corresponding amount of a substance, $C_7H_{12}O_2$, containing one hydroxyl group and forming a *mono*-p-*nitrobenzoate*. The second oxygen atom is neither hydroxylic nor ketonic, and is probably similar to the oxidic group in the isomeric form of ascaridole. The substance is stable in presence of potassium permanganate in neutral solution, but is readily oxidised by Beckmann's chromic acid mixture to the lactone of β-hydroxy-β-methyladipic acid (VII). It is therefore considered to be 1-*methyl*cyclo*hexan*-1-*ol* 3 : 4-*oxide* (VI).



(V.) (VI.) (VII.)

## Experimental.

In the following experiments Zerewitinoff determinations of replaceable hydrogen can indicate only the hydrogen in hydroxyl groups and are shown as "OH%." The quantity of titanous chloride used or of iodine liberated is shown in c.c. of N-solution required by 1 g. of the substance, the calculated value for ascaridole being based on the addition of 4 atoms of hydrogen. Thus, by the titanous chloride method of estimation (Paget, *loc. cit.*) 1 g. of ascaridole is equivalent to 8·25 c.c. of N-solution, and by the B.P. method to 15·05 c.c. (calc., 23·8 c.c.).

Although chenopodium oil decomposes explosively on heating, it can be fractionally distilled at reduced pressure. Ascaridole thus obtained had b. p. 112—115°/20 mm., $d_{18°}^{18°}$ 1·0074, $[\alpha]_D$ −2·3°. Estimated by titanous chloride, it contained 100% ascaridole (Found: 1 g. = 8·25 c.c. of N-solution). It was dissolved in 2 vols. of light petroleum (b. p. 40—60°) and cooled in solid carbon dioxide with gentle stirring until, at about −20°, a good crop of crystalline matter separated. The supernatant solution was removed by suction, and the solid recrystallised twice more in the same way. The final crop (43%), freed from solvent by distillation, had m. p. 2°, b. p. 113—114°/20 mm., $d_{18°}^{18°}$ 1·0114, $[\alpha]_D$ −0·03° [Found: by titanous chloride, 1 g. = 8·95 c.c. of N-solution; by B.P. method, 1 g. = 16·0 c.c. of N-solution; iodine absorption value (Wijs), 144·5. Calc. for ascaridole: 1 g. = 23·8 c.c. of N-solution; iodine absorption value, 151·2%]. It contained no replaceable hydrogen. These figures were not appreciably altered by crystallisation six more times from light petroleum or from 95% alcohol.

*Reduction by Titanous Chloride.*—Ascaridole (5 g.) in alcohol (5 c.c.) was added to a cold solution of 50 c.c. of titanous chloride (commercial 15% solution in 15% hydrochloric acid), diluted with 50 c.c. of water, and gently shaken while carbon dioxide was passed slowly through the flask. A gaseous product, which was collected over potassium hydroxide solution, amounted to 230 c.c. at N.T.P. It was wholly liquefied by cooling in solid carbon dioxide, and had b. p. −37·5°/754 mm. [Found: *M* (by density), 44·1. Calc. for propane: *M*, 44·0]. It reacted slowly with bromine in sunlight, without diminution of volume and with production of hydrogen bromide. The acid liquor was shaken with ether, and the extract washed successively with 1% solutions of sodium carbonate and sodium hydroxide. From the sodium carbonate washing was obtained by ether a small crystalline extract, which separated from benzene in colourless prisms, m. p. 191° [Found: C, 54·0; H, 8·55; Cl, 15·85; OH, 22·1. $C_{10}H_{16}Cl(OH)_3$ requires C, 53·9; H, 8·55; Cl, 15·95; OH, 22·9%]. It has not been possible, on the quantity available, to determine the constitution of this substance, but it has the composition of a *chlorotrihydroxymenthane*. A *mono*-p-*nitrobenzoate* was obtained from it, crystallising from chloroform in nearly colourless needles, m. p. 124° (Found: N, 3·7; Cl, 9·65. $C_{17}H_{22}O_6NCl$ requires N, 3·8; Cl, 9·55%). It was not reduced by catalytic hydrogenation, and it could not be prepared by addition of hypochlorous acid to $\Delta^3$-*p*-menthene-1 : 4-diol. It does not therefore afford indication of the formation of this substance as an intermediate reduction product, which,

as shown below, is a product of partial hydrogenation of ascaridole. The sodium hydroxide washings on acidification furnished *p*-cresol, which after distillation melted at 35° (Found: C, 78·0; H, 7·25. Calc.: C, 77·8; H, 7·4%). It was identified as the *p*-nitrobenzoate, m. p. 102° (Found: N, 5·55. Calc.: N, 5·45%), and α-naphthylurethane, m. p. 144° (Found: N, 5·1. Calc.: N, 5·1%). The yield of *p*-cresol was about 33%.

The oil remaining after washing with alkali still contained some chlorine and distilled only with decomposition. It was shaken with water, extracted once with light petroleum, and then exhaustively with ether. From the latter extract a small amount of an unsaturated *glycol* separated, crystallising in colourless needles, m. p. 84°, from chloroform–light petroleum [Found: C, 70·6; H, 10·6; OH, 17·3. $C_{10}H_{16}(OH)_2$ requires C, 70·6; H, 10·6; OH, 20·0%]. Admixture of $\Delta^2$-*p*-methene-1 : 4-diol (m. p. 82°) depressed the m. p. to 67—70°. In presence of Adams's platinnm oxide catalyst, it slowly absorbed 1 mol. of hydrogen (Found: 1 g. = 126 c.c. Required, 132 c.c.). The saturated *glycol* crystallised from benzene in white needles, m. p. 114°, depressed by admixture of *cis*-1 : 4-terpin (m. p. 117°), of terpin hydrate (m. p. 116°), or of *trans*-1 : 4-terpin (m. p. 137°).

The oily product from light petroleum and from ether was dissolved in dry pyridine and gently warmed with twice its weight (about 2 mols.) of *p*-nitrobenzoyl chloride, yielding an ester which, after crystallisation from ethyl acetate, melted at 174°, alone or mixed with *ascaridole α-glycol di*-p-*nitrobenzoate* (Found: C, 59·65; H, 5·0; N, 5·8. $C_{24}H_{24}O_9N_2$ requires C, 59·5; H, 5·0; N, 5·8%). *Ascaridole-α-glycol mono*-p-*nitrobenzoate*, prepared from ascaridole α-glycol and 1 mol. of *p*-nitrobenzoyl chloride in a similar way, formed colourless needles, m. p. 150°, from chloroform (Found: C, 61·0; H, 6·25; N, 4·3. $C_{17}H_{21}O_6N$ requires C, 60·9; H, 6·3; N, 4·2%). No further crystalline products were obtained from the syrupy residue.

*Hydrogenation of Ascaridole.*—Ascaridole (0·5 g.) in 10 c.c. of 95% alcohol was hydrogenated as described by Wallach (*loc. cit.*) (Found: 1 g. = 234 c.c. Calc. for $2H_2$, 266·6 c.c.), yielding *cis*-1 : 4-terpin, which was characterised by the preparation with *p*-nitrobenzoyl chloride in pyridine solution of a *mono*-p-*nitrobenzoate*, which formed pale yellow prisms, m. p. 117°, from methyl alcohol (Found: C, 63·7; H, 7·45; N, 4·65. $C_{17}H_{23}O_5N$ requires C, 63·55; H, 7·15; N, 4·35%), and a *di*-p-*nitrobenzoate*, which crystallised in pale yellow needles, m. p. 172°, from methyl alcohol–benzene (Found: C, 61·45; H, 5·7; N, 6·2. $C_{24}H_{26}O_8N_2$ requires C, 61·3; H, 5·5; N, 5·95%).

Ascaridole (20 g.) in 95% alcohol (20 c.c.) was hydrogenated in presence of 0·1 g. of Adams's platinum oxide catalyst, until the point was reached at which the rate of absorption slackened, corresponding with the addition of 1 mol. (Found: 1 g. = 134·0 c.c.). The product after filtration and removal of the solvent crystallised from 2 vols. of light petroleum cooled in ice-salt. *Dihydroascaridole* was thus obtained, m. p. 19·5°, b. p. 112—115°/18 mm., $[\alpha]_D \pm 0°$ (Found: C, 71·0; H, 10·8. $C_{10}H_{18}O_2$ requires C, 70·6; H, 10·6%). It contained no replaceable hydrogen and did not absorb iodine by the Wijs process, but was readily reduced by titanous chloride (Found: 1 g. = 10·6 c.c. of N-solution. Required, 11·8 c.c.). On further hydrogenation dihydroascaridole yielded *cis*-1 : 4-terpin quantitatively.

When ascaridole was partly hydrogenated in presence of palladised charcoal instead of platinum oxide (Richter and Presting, *loc. cit.*), and the product digested with light petroleum, a part (47%) was insoluble. Crystallised from light petroleum–chloroform, it had m. p. 82°, $[\alpha]_D \pm 0°$ [Found: C, 70·6; H, 10·85; OH, 20·65; iodine absorption value (Wijs), 132·0. Calc. for $C_{10}H_{16}(OH)_2$: C, 70·6; H, 10·6; OH, 20·0%; iodine absorption value, 149·3%], and is no doubt $\Delta^2$-*p*-methene-1 : 4-diol. It was not reduced by titanous chloride. The *di*-p-*nitrobenzoate* crystallised from methyl alcohol in pale yellow needles, m. p. 130° (Found: C, 61·4; H, 5·4; N, 6·2. $C_{24}H_{24}O_8N_2$ requires C, 61·55; H, 5·1; N, 6·0%). The fraction of the reduction product which was soluble in light petroleum, after concentration and cooling in a freezing mixture, yielded dihydroascaridole (23%).

*Reduction of Dihydroascaridole by Titanous Chloride.*—Dihydroascaridole (5 g.) was treated with a solution of titanous chloride in an atmosphere of carbon dioxide as already described above. A gaseous product was evolved (601 c.c.), which was identified as propane [*M* (by density), 43·1. Yield, 91%]. The liquors were thoroughly extracted by ether, yielding an oil (3·5 g.), which distilled without decomposition, was readily soluble in water, and crystallised from *iso*propyl ether in colourless rods, m. p. 45°, b. p. 110°/5 mm. [Found: C, 65·7; H, 9·4; OH, 12·8. $C_7H_{11}O(OH)$ requires C, 65·6; H, 9·4; OH, 13·3%]. No semicarbazone could be obtained, but it gave a *mono*-p-*nitrobenzoate*, crystallising from *iso*propyl ether–ethyl acetate in yellow leaflets, m. p. 157° (Found: C, 60·7; H, 5·5; N, 5·05. $C_{14}H_{15}O_5N$ requires C, 60·6; H, 5·4; N, 5·05%). This substance is considered to be 1-*methyl*cyclo*hexan*-1-*ol* 3 : 4-*oxide* (VI)

It was not attacked by potassium permanganate in acetone solution, but was (2·0 g.) rapidly oxidised by Beckmann's chromic acid mixture (50 c.c.), yielding a lactone acid (2·3 g.), readily soluble in water. In cold aqueous solution 0·1858 g. was neutralised by 11·7 c.c. of N/10-baryta ($M$ = 158·8. Calc. for $C_6H_9O_2{\cdot}CO_2H$, 158) and, on heating with an excess of baryta, by 23·5 c.c. The barium salt was readily soluble in water (Found: Ba, 44·6. Calc. for $C_7H_{10}O_6Ba$: Ba, 44·1%). The acid crystallised after some days in a vacuous desiccator in hygroscopic prisms, m. p. 49—52°, and this was not altered by admixture with a specimen of β-hydroxy-β-methyladipic acid lactone, prepared by the method of Duden and Freydag (*Ber.*, 1903, **36**, 953), which crystallised in the same way in a vacuous desiccator and melted at 50—52°.

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The Wellcome Chemical Research Laboratories,
London, N.W. 1. [*Received, April 14th*, 1938.

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## 161. 2 : 6-*Dimethyl Glucose.*

By D. J. Bell and R. L. M. Synge.

4 : 6-*Ethylidene* β-*methylglucoside* 3-*nitrate*, subjected to reactions described by Bell and Synge (J., 1937, 1711), yielded β-*methylglucoside* 3 : 4-*dinitrate*. This was methylated to give the 2 : 6-*dimethyl* derivative, from which crystalline 2 : 6-*dimethyl* β-*methylglucoside* was prepared. The constitution of this was proved by preparation of its known di-*p*-toluenesulphonate (Oldham and Rutherford, *J. Amer. Chem. Soc.*, 1932, **54**, 1086). The free *sugar* was then prepared; as it did not crystallise, it was characterised by conversion into the corresponding *dimethyl gluconophenylhydrazide*. Eight new crystalline derivatives of β-methylglucoside are described.

For a number of years one of us has made attempts to prepare 2 : 6-*dimethyl glucose*, with a view to its employment in polysaccharide chemistry. The two methods already described (Bell, J., 1935, 175; 1936, 186) gave the desired dimethyl sugar accompanied by so great a preponderance of isomers that its separation was impossible in any form other than 3 : 4-di-*p*-toluenesulphonyl 2 : 6-dimethyl β-methylglucoside (Oldham and Rutherford, *J. Amer. Chem. Soc.*, 1932, **54**, 1086), a derivative from which it has not, so far, been regenerated.

Two circumstances have now combined to enable us to attain our end. First, in a private communication, Dr. J. W. H. Oldham has informed us that the action of sodium iodide in acetone on 4 : 6-ethylidene β-methylglucoside 2 : 3-dinitrate leads to the production of 4 : 6-*ethylidene* β-*methylglucoside* 3-*nitrate*. (A full description of the application of this reaction to other sugar nitrates is in course of preparation by Dr. Oldham. The present authors wish here to express their indebtedness to him; by his friendly co-operation this work was made possible.) Secondly, we have been able to show that acetic anhydride containing 0·1% of sulphuric acid can effect an opening at $C_6$ of the 1 : 3-dioxan ring of 4 : 6-ethylidene β-methylglucoside derivatives (Bell and Synge, J., 1937, 1711; following paper), leading to certain synthetically useful substitution reactions involving $C_4$ and $C_6$.

The reactions studied in the course of this work are summarised below, where B signifies β-methylglucoside.

The constitution of the new sugar is evident from the following considerations: (1) Non-migration of nitrate groups being assumed, one methyl group must be in position 2, since authentic 2-methyl β-methylglucoside yields the same ethylidene derivative as was obtained by methylating the mononitrate of 4 : 6-ethylidene β-methylglucoside used as starting material. This confirms the position of esterification in the latter as $C_3$. (2) The 3 : 4-di-*p*-toluenesulphonyl 2 : 6-dimethyl β-methylglucoside obtained in this research is identical with the synthetic product of Oldham and Rutherford (*loc. cit.*), which was

obtained from 2-methyl β-methylglucoside by introduction of methyl into position 6 by a generally applicable method.

4 : 6-Ethylidene B 2 : 3-dinitrate
↓
4 : 6-Ethylidene B 3-nitrate ⟶ 4 : 6-*Ethylidene 2-methyl B 3-nitrate*
↓ ↓
4 : 6-*Ethylidene 2-methyl B* ⟵ 2-Methyl B
2 : 6-*Diacetyl 4-α-acetoxyethyl B 3-nitrate* ↘
2 : 6-*Dimethyl B 3 : 4-dinitrate* ⟵ *B 3 : 4-dinitrate* ⟵ 2 : 6-*Diacetyl B 3 : 4-dinitrate*
↓
2 : 3-*Dimethyl B* ⟶ 3 : 4-Di-*p*-toluenesulphonyl 2 : 6-dimethyl B
↓
2 : 6-Dimethyl glucose ⟶ 2 : 6-Dimethyl gluconolactone (not characterised)
↓
2 : 6-*Dimethyl gluconophenylhydrazide*

Sodium methoxide is used to remove catalytically the two acetyl groups from 2 : 6-diacetyl β-methylglucoside 3 : 4-dinitrate, readily converting it into β-methylglucoside 3 : 4-dinitrate. It is noteworthy that the same treatment applied to 6-acetyl β-methylglucoside 2 : 3 : 4-trinitrate is without effect (Bell and Synge, 1937, *loc. cit.*). Possibly in each case an equilibrium is reached, but in the latter the free energy of "*Umesterung*" is such that the reaction does not proceed far. This view is supported by the fact that the mother-liquors from the crystallisation of β-methylglucoside 3 : 4-dinitrate yield on evaporation an uncrystallisable residue, from which by repeated treatment with sodium methoxide a further crop of crystalline β-methylglucoside 3 : 4-dinitrate can be obtained. This behaviour is intermediate between that of 6-acetyl β-methylglucoside 2 : 3 : 4-trinitrate and that of 4 : 6-diacetyl β-methylglucoside 2 : 3-dinitrate (Bell and Synge, 1937, *loc. cit.*), which is converted quantitatively into the corresponding dinitrate on treatment with sodium methoxide under the same conditions.

## EXPERIMENTAL.

Unless otherwise stated, all evaporations were carried out under reduced pressure and below 50°. Substances were recrystallised until a constant m. p. was attained.

4 : 6-*Ethylidene β-Methylglucoside 3-Nitrate* (I).—Despite various experimental modifications, this reaction gave uncertain results. The best yield was obtained thus: 2 g. of 4 : 6-ethylidene β-methylglucoside 2 : 3-dinitrate (Oldham, unpnblished work; Bell and Synge, J., 1937, 1711) were heated for 1 hr. in a sealed tube with 1 g. of sodium iodide and 20 ml. of acetone at 100°. After cooling, the product was mixed with chloroform, and washed first with sodium thiosulphate solution and then with concentrated potassium bicarbonate solution; after drying (sodium sulphate), the colourless chloroform solution was evaporated to dryness, and the crystalline residue was recrystallised first from a small quantity of ether and then from ethyl alcohol. Yield, 1·2 g. (needles), m. p. 135—140°. The pure *nitrate*, obtained by recrystallisation from methyl alcohol, had m. p. 146—148°, $[\alpha]_D^{18°}$ −30·8° ($l$ = 2, $c$ = 1·8 in chloroform) (Found: C, 41·1; H, 5·5; N, 5·0; OMe, 11·7. $C_9H_{15}O_8N$ requires C, 40·8; H, 5·7; N, 5·3; OMe, 11·7%).

4 : 6-*Ethylidene 2-Methyl β-Methylglucoside 3-Nitrate* (II).—2·7 G. of (I), treated with Purdie's reagents, gave 2·7 g. of pure *product*, which, recrystallised from light petroleum (b. p. 60—80°), formed prisms, m. p. 104·5—105·5° after softening at 101°, $[\alpha]_D^{18°}$ −28·7° ($l$ = 2, $c$ = 3·3

in chloroform) (Found: C, 43·9; H, 6·4; N, 4·9; OMe, 22·0. $C_{10}H_{17}O_8N$ requires C, 43·0; H, 6·1; N, 5·0; OMe, 22·2%).

4 : 6-*Ethylidene 2-Methyl β-Methylglucoside* (III).—(a) *From* (II). Reduction of (II) by alcoholic sodium sulphide, followed by extraction of the reaction mixture by chloroform in the usual way, gave a 97% yield of nitrate-free, fine needles. After recrystallisation from ether, these had m. p. 122—123°, $[\alpha]_D$ −66·0° ($l$ = 2, $c$ = 2 in chloroform) (Found: C, 51·2; H, 7·5; OMe, 26·2. $C_{10}H_{18}O_6$ requires C, 51·3; H, 7·7; OMe, 26·5%).

(b) *From pure 2-methyl β-methylglucoside* (Oldham, *J. Amer. Chem. Soc.*, 1934, **56**, 1360), m. p. 94—96°. The glucoside, added to 10 parts of paraldehyde (dried over calcium chloride) containing 1% of sulphuric acid, dissolved immediately. After keeping at 0° for 12 hrs., excess of sodium bicarbonate solution was added, and the whole evaporated to dryness. The residue was dissolved in water, and the solution extracted six times with chloroform. The product crystallised from the extract and on recrystallisation from ether formed fine needles, having m. p. 122°, not depressed by the specimen obtained in (a), $[\alpha]_D^{17°}$ −64·0° ($l$ = 2, $c$ = 2 in chloroform).

2 : 6-*Diacetyl 4-α-Acetoxyethyl β-Methylglucoside 3-Nitrate* (IV).—A solution of 2·5 g. of (I) in 50 ml. of acetic anhydride containing 0·05 ml. of sulphuric acid was observed polarimetrically until the rotation reached a steady value (30 mins.). It was then poured into 250 ml. of water containing some sodium acetate, and was stirred until the acetic anhydride had decomposed, crystals being meanwhile deposited. The whole was extracted thrice with benzene, and the extract, after drying (sodium sulphate), evaporated. A solution of the residue in hot alcohol deposited crystals on cooling. The mother-liquor from these was evaporated, and the syrupy residue subjected again to acetolytic treatment. A further small quantity of crystals was obtained on working up as before. Recrystallised from alcohol, the *substance* (1·85 g.) had m. p. 125—126° after softening at 124°, $[\alpha]_D^{20°}$ + 13·4° ($l$ = 2, $c$ = 4·8 in chloroform) (Found: C, 44·3; H, 5·7; N, 3·6. $C_{15}H_{23}O_{12}N$ requires C, 44·0; H, 5·6; N, 3·4%).

2 : 6-*Diacetyl β-Methylglucoside* 3 : 4-*Dinitrate* (V).—5·9 G. of (IV) were treated with fuming nitric acid in chloroform and worked up in the usual manner (Bell and Synge, 1937, *loc. cit.*). The syrup obtained deposited crystals from alcohol, giving 3·7 g. in the first crop. The mother-liquors on concentration yielded no more crystals, but on repetition of the treatment with nitric acid on the evaporated residue a further 0·3 g. of crystals was obtained. The *substance* formed needles, m. p. 90—91°, $[\alpha]_D^{20°}$ −27·3° ($l$ = 2, $c$ = 2·9 in chloroform) (Found: C, 36·95; H, 4·3; N, 8·2; OMe, 8·3. $C_{11}H_{16}O_{12}N_2$ requires C, 35·85; H, 4·35; N, 7·6; OMe, 8·4%).

*β-Methylglucoside* 3 : 4-*Dinitrate* (VI).—4·0 G. of (V) were treated for 1 hr. at room temperature in 10 ml. of chloroform with a freshly prepared solution of 3 mg. of sodium in 10 ml. of methyl alcohol. After neutralisation with acetic acid the solution was evaporated to dryness, and the product extracted with ether. Addition of chloroform to the residue from the evaporation of the ether produced an immediate crop of fine needles, which, after recrystallisation from hexane–chloroform (1 : 1), gave 2·6 g., m. p. 116—118°. A second treatment with sodium methoxide of the uncrystallisable residue in the mother-liquors yielded 0·4 g. more of crystalline *product*, $[\alpha]_D^{16°}$ +13·9° ($l$ = 2, $c$ = 3 in methyl alcohol) (Found: C, 29·7; H, 4·1; N, 9·8; OMe, 10·8. $C_7H_{12}O_{10}N_2$ requires C, 29·55; H, 4·2; N, 9·5; OMe, 10·9%).

2 : 6-*Dimethyl β-Methylglucoside* 3 : 4-*Dinitrate* (VII).—0·25 G. of (VI) was methylated three times with Purdie's reagents; 0·28 g. of crystals were obtained from methyl alcohol, m. p. 74—76°, $[\alpha]_D^{20°}$ −13·7° ($l$ = 2, $c$ = 7·5 in chloroform) (Found: C, 34·7; H, 5·4; N, 8·9; OMe, 29·1. $C_9H_{16}O_{10}N_2$ requires C, 34·6; H, 5·1; N, 9·0; OMe, 29·8%).

2 : 6-*Dimethyl β-Methylglucoside* (VIII).—2·4 G. of (VII) in 24 ml. of alcohol were heated at 100° for 30 mins. with 24 ml. of 30% sodium hydroxide solution which had been saturated with hydrogen sulphide. After the alcohol had been distilled, much potassium carbonate was added and the solution was extracted nine times with chloroform. The chloroform extracts were dried (sodium sulphate) and evaporated, and the residual syrup was distilled at 150°/0·05 mm. The residue was negligible, and the distillate crystallised on trituration with ether. Recrystallisation from ether–hexane in the cold gave 1·3 g. of fine needles (slightly hygroscopic), m. p. 50—52°, $[\alpha]_D^{20°}$ −43·5° ($l$ = 2, $c$ = 10·8 in chloroform) (Found: C, 47·6; H, 8·2; OMe, 41·3. $C_9H_{18}O_6$ requires C, 48·6; H, 8·1; OMe, 41·8%).

p-*Toluenesulphonylation of* (VIII).—0·20 G. was treated in the usual way, and on being worked up, the crude product crystallised; recrystallisation from alcohol gave needles, m. p. 156—158° alone or mixed with authentic 3 : 4-di-*p*-toluenesulphonyl 2 : 6-dimethyl β-methylglucoside, m. p. 156—158° (Oldham and Rutherford, *loc. cit.*). These authors and Bell (J., 1936, 186) record $[\alpha]_D$ in chloroform −8·8° and −8·9° respectively. Our specimen had $[\alpha]_D^{18°}$ −

−8·2° ($l$ = 2, $c$ = 8 in chloroform) (Found: C, 52·3; H, 6·0; S, 11·3; OMe, 18·6. Calc. for $C_{23}H_{30}O_{10}S_2$: C, 52·1; H, 5·7; S, 12·1; OMe, 17·55%).

2 : 6-*Dimethyl Glucose* (IX).—1·20 G. of (VIII) were heated at 100° with 20 ml. of 0·6N-hydrochloric acid until a constant polarimetric reading was obtained (7 hrs.). After neutralisation by lead carbonate the product was worked up as in the preparation of 4 : 6-dimethyl glucose (Bell and Synge, 1937, *loc. cit.*), 1·0 g. of a colourless glass being obtained. This could not be crystallised. $[\alpha]_D^{17°}$ +58·3° (constant for 12 hrs.) ($l$ = 2, $c$ = 2·7 in water) (Found: OMe, 29·8. $C_8H_{16}O_6$ requires OMe, 29·8%).

2 : 6-*Dimethyl Gluconophenylhydrazide.*—Oxidation of (IX) to the corresponding dimethyl gluconolactone was carried out by the method of Hudson and Isbell (*J. Amer. Chem. Soc.*, 1929, **51**, 2225), the manner of working up being slightly modified. To 0·88 g. of (IX), dissolved in 38 ml. of water, were added 3·3 g. of barium benzoate and 0·3 ml. of bromine. The mixture was shaken well, and kept in the dark until all reducing power (Fehling's solution) had disappeared (24 hrs.). After removal of all bromine by aëration, an exact equivalent of sulphuric acid was added to precipitate the barium, and the mixture was heated at 100° for ½ hr. When cool, the mixture was centrifuged, and the centrifugate was extracted three times with benzene to remove benzoic acid. (Owing to the breaking of a tube on the centrifuge, a loss of about 25% occurred at this stage.) Bromide was then eliminated by treatment with silver oxide, and silver was removed from the resulting filtrate by treatment with hydrogen sulphide. Evaporation of the clear filtrate from the silver sulphide yielded an almost colourless, non-reducing syrup, which was freed from traces of inorganic material by solution in chloroform, followed by filtration. This filtrate was evaporated, and the residue heated for 5 hrs. at 100°/0·01 mm. Yield, 0·46 g. of a syrup which did not crystallise, but displayed the expected solubilities of a dimethyl hexonolactone.

To a solution of this in dry ether was added 0·3 g. of freshly distilled phenylhydrazine. Almost immediately an oil separated. As this did not crystallise overnight, the mixture was boiled under reflux for 2 hrs.; crystallisation then commenced. Recrystallised from alcohol–ether–light petroleum, fine needles were obtained (0·2 g.), m. p. 127—129°, $[\alpha]_D^{17°}$ +48·6° ($l$ = 2, $c$ = 3 in ethyl alcohol) (Found: C, 53·4; H, 7·0; N, 10·0; OMe, 20·4. $C_{14}H_{22}O_6N_2$ requires C, 53·5; H, 7·0; N, 8·9; OMe, 19·7%).

This work was carried out during the tenure by one of us (R. L. M. S.) of the Benn W. Levy Studentship.

BIOCHEMICAL LABORATORY, CAMBRIDGE. [*Received, April 6th*, 1938.]

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## 162. *β-Methylglucoside 2 : 3 : 6-Trinitrate.*

By D. J. BELL and R. L. M. SYNGE.

*β-Methylglucoside 2 : 3 : 6-trinitrate* has been synthesised from β-methylglucoside 2 : 3-dinitrate, and its constitution proved by methylation.

Further evidence is brought forward supporting the formulation of the compound described (Bell and Synge, J., 1937, 1711) as 6-acetyl 4-α-acetoxyethyl β-methylglucoside 2 : 3-dinitrate.

Two new crystalline derivatives of β-methylglucoside are described.

IN a previous paper (*loc. cit.*) we announced our intention of preparing a glucose derivative substituted in positions 2, 3, and 6 by the nitrate group. We have now succeeded in preparing β-*methylglucoside* 2 : 3 : 6-*trinitrate*, which we hope will be of use for synthetic work involving substitution of glucose residues at position 4.

The following series of reactions was employed: β-methylglucoside 2 : 3-dinitrate (Bell and Synge, *loc. cit.*) was condensed with triphenylchloromethane to yield its 6-triphenylmethyl ether, which could not be crystallised. Acetylation of this compound gave crystalline 4-*acetyl* 6-*triphenylmethyl* β-*methylglucoside* 2 : 3-*dinitrate*, which, on treatment with fuming nitric acid in chloroform (cf. Oldham and Bell, *J. Amer. Chem. Soc.*, 1938, **60**, 323), was converted into crystalline 4-*acetyl* β-*methylglucoside* 2 : 3 : 6-*trinitrate*. This, on treatment with sodium methoxide, gave a quantitative yield of

*β-methylglucoside 2 : 3 : 6-trinitrate* as a colourless glass which could not be made to crystallise. The overall yield from β-methylglucoside 2 : 3-dinitrate was about 30%, which corresponds to an overall yield from β-methylglucoside of about 15%.

The constitution of the β-methylglucoside trinitrate was proved by methylation, which, since no case of migration of the nitrate group has yet been reported, we consider to be a valid method. By this means we obtained a syrup having a methoxyl content agreeing with the theoretical for a monomethyl β-methylglucoside trinitrate. Reductive removal of nitrate from this, followed by acetylation, gave a fair yield of crystalline 2 : 3 : 6-triacetyl 4-methyl β-methylglucoside. Our specimen, which, owing to the small quantities with which we were working, could not be completely purified, had m. p. 105—106° and $[\alpha]_D^{20°}$ — 34·9° ($l$ = 2, $c$ = 2·5 in chloroform). We were unable to obtain a specimen of authentic 2 : 3 : 6-triacetyl 4-methyl β-methylglucoside (Levene and Raymond, *J. Biol. Chem.*, 1932, **97**, 763; Munro and Percival, J., 1935, 873) for a mixed melting point determination, but Professor B. Helferich of Leipzig kindly gave us a specimen of 2 : 3 : 4-triacetyl 6-methyl β-methylglucoside, which depressed the melting point of our compound by more than 20°. The four theoretically possible triacetyl methyl β-methylglucopyranosides are all known, and are tabulated below. Comparison of our compound with those listed leaves no doubt as to its identity.

*The triacetyl methyl β-methylglucopyranosides.*

| Position of Me. | M. p. | $[\alpha]_D$ (chloroform). | Authors. |
|---|---|---|---|
| 2 | 74—75° | + 6·3° | Brigl and Schinle, *Ber.*, 1929, **62**, 1716. |
| 3 | 90—90·5 | —34·8 | Helferich and Lang, *J. pr. Chem.*, 1932, **132**, 321. |
| 4 | 107—108 | —32·8 | Levene and Raymond, *loc. cit.* |
| | 106 | —34·0 | Munro and Percival, *loc. cit.* |
| 6 | 107—108 | —12·4 | Helferich and Himmen, *Ber.*, 1929, **62**, 2141; Helferich and Günther, *Ber.*, 1931, **64**, 1276. |

The fact that 4-acetyl β-methylglucoside 2 : 3 : 6-trinitrate has quite different properties from the compound formulated by us (Bell and Synge, *loc. cit.*) as 6-acetyl β-methylglucoside 2 : 3 : 4-trinitrate corroborates our proposed structure for the latter compound, and consequently our view that the 1 : 3-dioxan ring of the parent ethylidene compound is opened by acetolysis at $C_6$ of the glucose chain. An entirely analogous reaction of 4 : 6-ethylidene β-methylglucoside 3-nitrate is described in the preceding paper, and serves as further confirmation.

An attempt to *p*-toluenesulphonylate β-methylglucoside 2 : 3 : 6-trinitrate was unsuccessful. We were previously unable (*loc. cit.*) to *p*-toluenesulphonylate the product of mild acid hydrolysis of 6-acetyl 4-α-acetoxyethyl β-methylglucoside 2 : 3-dinitrate, which probably consists largely of 6-acetyl β-methylglucoside 2 : 3-dinitrate, a compound of similar structure.

## Experimental.

Unless otherwise stated, evaporations were carried out under reduced pressure and below 50°, and substances were recrystallised until a constant m. p. was attained.

*6-Triphenylmethyl β-Methylglucoside 2 : 3-Dinitrate* (I).—5·8 G. of β-methylglucoside 2 : 3-dinitrate and 6·45 g. of freshly prepared triphenylchloromethane were dissolved in the minimum quantity of pyridine which had been dried with phosphoric oxide, and kept for 7 days at 37° in a stoppered flask. The mixture was then poured into water. A gum separated, and was removed by extraction with benzene. The benzene was washed twice with water, dried (sodium sulphate), and evaporated to dryness. Water was repeatedly added to the residue and evaporated, until there was no smell of pyridine; 9·7 g. of syrup were obtained, which could not be crystallised.

*4-Acetyl 6-Triphenylmethyl β-Methylglucoside 2 : 3-Dinitrate* (II).—The syrup was dissolved in 100 ml. of pyridine–acetic anhydride (1 : 1) and kept at room temperature for 24 hrs., and the mixture then poured into water. The precipitated oil soon became a stiff crystalline mass, which was recrystallised from alcohol, giving 6·1 g. of crystals, m. p. 153—155°, $[\alpha]_D^{18°}$ + 31·8° ($l$ = 2, $c$ = 2 in chloroform) (Found: C, 59·0; H, 4·75; N, 4·9; OMe, 5·6. $C_{28}H_{28}O_{11}N_2$ requires C, 59·1; H, 4·9; N, 4·85; OMe, 5·45%).

An attempt to shorten the procedure by adding acetic anhydride to the original reaction mixture before (I) had been submitted to benzene extraction led to extensive formation of 4 : 6-diacetyl β-methylglucoside 2 : 3-dinitrate (Bell and Synge, *loc. cit.*), from which (II) could not easily be separated. The procedure finally adopted eliminates all unchanged β-methylglucoside 2 : 3-dinitrate prior to acetylation.

*4-Acetyl β-Methylglucoside 2 : 3 : 6-Trinitrate* (III).—1 G. of (II) was dissolved in 10 ml. of chloroform, and treated for 10 mins. at 0° with 20 ml. of chloroform–fuming nitric acid (1 : 1). The mixture was poured into excess of ice-water, and the chloroform layer separated, washed with potassium bicarbonate solution, dried (sodium sulphate), and evaporated to dryness. A crystalline mass was obtained, largely a mixture of (III) with triphenylcarbinol. A preliminary experiment with the latter showed that, when dissolved in ether, it is not precipitated by the addition of 3 vols. of hexane. Application of this treatment to a concentrated ethereal solution of the reaction product caused (III) to crystallise immediately in large needles, which could then easily be purified by recrystallisation from alcohol. Crystallisation from alcohol of the material remaining in the ether–hexane solution gave mainly triphenylcarbinol, and when the alcoholic mother-liquors from the crystallisation of this were combined with those from (III), a further yield of (III) could be obtained by repeating the ether–hexane treatment on this mixture. By these means 0·35 g. was obtained, m. p. 94—95°, $[\alpha]_D^{19°}$ + 0·4° ($l$ = 2, $c$ = 3 in chloroform) (Found: C, 30·45, 31·0; H, 3·5, 3·9; N, 10·65; OMe, 8·75; *M*, cryoscopic in acetic acid, 353. $C_9H_{13}O_{13}N_3$ requires C, 29·1; H, 3·5; N, 11·3; OMe, 8·4%; *M*, 371).

*β-Methylglucoside 2 : 3 : 6-Trinitrate* (IV).—0·29 G. of (III) was dissolved in 3 ml. of chloroform, and 3 ml. of methyl alcohol, in which 5 mg. of sodium had been dissolved immediately beforehand, were added. After ½ hr., a drop of acetic acid was added, and the mixture evaporated to dryness. The residue was extracted with ether, and the extracts filtered through charcoal and evaporated to dryness. Yield, 0·25 g. of a colourless glass, which could not be crystallised from ether–hexane or from alcohol, or by keeping over phosphoric oxide for a month (Found: OMe, 8·9. $C_7H_{11}O_{12}N_3$ requires OMe, 9·4%).

The *product* (IV), when treated with *p*-toluenesulphonyl chloride in pyridine under the usual conditions, yielded a syrup [only 30% of the weight of (IV) employed] which could not be crystallised.

*4-Methyl β-Methylglucoside 2 : 3 : 6-Trinitrate.*—0·2 G. of (IV) on double treatment with silver oxide and methyl iodide yielded 0·21 g. of a colourless syrup which could not be crystallised (Found: OMe, 17·9. $C_8H_{13}O_{12}N_3$ requires OMe, 18·1%).

*2 : 3 : 6-Triacetyl 4-Methyl β-Methylglucoside.*—The above syrup was dissolved in 2 ml. of acetic acid and treated with iron filings and zinc dust over a free flame until no further brown fumes were evolved. Water was added, and then sodium carbonate equivalent to the acetic acid used. The precipitate obtained was washed with water, and the combined filtrate and washings were evaporated to dryness under reduced pressure at 100°. 25 Ml. of acetic anhydride were added and the mixture was heated for a short time on a boiling water-bath and for 5 minutes over a free flame; it was then poured into excess of cold water, and the acetic acid resulting was neutralised with calcium carbonate. The precipitate was collected and washed with chloroform, which was subsequently used for extracting the filtrate. The combined chloroform extracts were dried (sodium sulphate) and evaporated to dryness, giving 0·13 g. of residue, which shortly crystallised in needles. Recrystallisation of this from ether–hexane gave 0·10 g. of crystalline material, which, owing to the small quantity available, was not further recrystallised. The m. p. and rotation are given above (Found: C, 50·7; H, 6·5; OMe, 18·8. Calc. for $C_{14}H_{22}O_9$: C, 50·3; H, 6·6; OMe, 18·6%).

This work was carried out during the tenure by one of us (R. L. M. S.) of the Benn W. Levy Studentship.

BIOCHEMICAL LABORATORY, CAMBRIDGE [*Received, April 6th*, 1938.

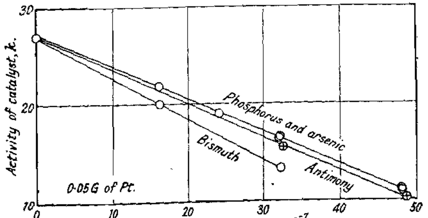
# 163. *Catalytic Toxicity and Chemical Structure. Part IV. The Relative Toxicity of Simple Phosphorus, Arsenic, Antimony, and Bismuth Compounds.*

By Edward B. Maxted and Arthur Marsden.

The simple hydrides of phosphorus and of arsenic—applied either as such or as compounds which, in the presence of catalytically activated hydrogen, are transformed into simple hydrides—possess the same toxicity per g.-atom of catalytically poisonous element towards a platinum catalyst in catalytic hydrogenation. The toxicity of antimony hydride is slightly, but not very appreciably, greater; and that of bismuth is definitely greater, the observed relative values of the poisoning coefficients per g.-atom being 1·0, 1·0, 1·05, and 1·29 for the series of four elements in the above order.

In earlier papers (J., 1937, 603, 1004; this vol., p. 455), attention has been paid principally to the development of induced toxicity in complex, but normally non-toxic, molecular structures as a result of their attachment to a catalysing surface by an intrinsically poisonous constituent such as a sulphur atom. Little is known, from a quantitative standpoint, of the effect on the toxicity of variations in the atomic radius of the catalytically poisonous element itself, such as would be introduced, for instance, by changing the identity of this element within a closely related periodic group. In examining this point experimentally, it is desirable to employ the simplest possible toxic molecules in order to avoid the above complication of induced toxicity; and a suitable series of corresponding compounds for the purpose appeared to be constituted by the simple hydrides of the phosphorus group, all of which are highly toxic towards, for instance, platinum in catalytic hydrogenation.

If the adsorption of simple poisons of this type occurs stoicheiometrically, *i.e.*, if each potentially catalytically active platinum surface element binds a single poison molecule—or a given number of poison molecules—it would be expected on first principles that the toxicity per g.-atom of all the related poisonous elements would be identical, so far as considerations of overlapping coverage, due to the possession by the poison of a larger effective atomic radius than that of the adsorbing element, do not actively restrict the possibility of normal close coverage of the catalysing surface by the poison. Thus, in the simplest case, if this postulated stoicheiometric adsorption corresponds with the adsorption of a single poison atom by each platinum surface element, the toxicity of all members of the poison series should be the same up to a stage in the series at which the effective atomic radius of the poison exceeds that of the platinum.




In the course of the measurements described in the present paper, a simple relationship of the above nature among the various toxicities per g.-atom of the respective poisons has been shown experimentally to be actually followed, in that phosphorus and arsenic—which possess, respectively, effective atomic radii of 0·87 and 1·25 A., compared with an atomic radius of 1·38 in the case of platinum—have been found, in each case in the form

of their trihydride, to possess the same atomic toxicity: moreover, although the atomic toxicity of antimony (atomic radius 1·45 A.), also as the hydride, differs little from that of phosphorus or arsenic, its value is apparently slightly higher than that of these elements; and, on still further increasing the atomic radius of the poison, by extending the measurements to bismuth (atomic radius 1·55 A.), the increase in atomic toxicity becomes sufficiently great to be readily measurable, although, as would be expected, the difference in toxicity is still not great.

## Experimental.

The determination of toxicity was carried out as already described in earlier papers of the present series, *viz.*, by measuring the activity of a standard platinum catalyst, of known poison content, for the hydrogenation of crotonic acid under standardised conditions. The system taken for hydrogenation consisted in each case of 0·05 g. of platinum, 5 c.c. of a 2N-solution of crotonic acid in acetic acid, and a known quantity of the poison dissolved in a further 5 c.c. of the same solvent. The platinum was, as before, taken from the same stock throughout, and had been prepared by the reduction of chloroplatinic acid with alkaline formate. The temperature of hydrogenation was 25°.

In preparing the various poisoning solutions, known quantities of compounds either containing the hydride itself or of such a nature that the hydride was produced *in situ* were weighed out and, after suitable dilution, applied to the platinum in the usual manner. In the case of phosphorus, the hydride could be weighed directly as phosphonium iodide, but arsenic and antimony hydrides, on the other hand, are less easy to handle as such. Since soluble arsenic or antimony compounds are readily transformed into the hydride by nascent or catalytically activated hydrogen, it was, however, found sufficient to weigh out these poisons in the form, respectively, of arsenious oxide and potassium antimonyl tartrate, which, in the presence of hydrogen and platinum, pass into the required hydride. The application of bismuth as the hydride is perhaps less definite. Paneth and Winternitz (*Ber.*, 1918, **51**, 1728) have observed the formation of a hydride, for instance, by dissolving a magnesium-bismuth alloy in acids; but it was considered preferable to employ as the poisoning solution in this case a dilute solution of bismuth acetate in acetic acid, since in all probability any soluble bismuth salt, in the presence of hydrogen and of platinum sufficient for adsorption of the poison, would be reduced to hydride in an analogous manner to arsenic and antimony; and, in any case, the bismuth was present in a molecularly simple form. These strong catalyst poisons, as was found with the sulphur compounds previously investigated, are, in the proportions used, substantially completely adsorbed by the platinum present. The final poisoning solutions contained, respectively, 0·0497 mg. P, 0·1201 mg. As, 0·1951 mg. Sb, and 0·3348 mg. Bi per c.c.

The effect of various quantities of each of these poisons on the activity of 0·05 g. of platinum is summarised in the figure. From the slope of these poisoning graphs, the poisoning coefficients, $\alpha$, may be calculated, as before, by means of the relationship $k_c = k_0(1 - \alpha c)$, in which $k_c$ is the activity of the platinum in the presence of a concentration, $c$, of the poison in question, and $k_0$ is the original, unpoisoned activity. If the poison concentrations are expressed in g.-atoms per unit of effective surface represented by that exposed by the 0·05 g. of the standard platinum catalyst taken in each case, the following values are obtained.

| Inhibitant. | $\alpha \times 10^{-5}$. | Relative toxicity per g.-atom of poison. | Inhibitant. | $\alpha \times 10^{-5}$. | Relative toxicity per g.-atom of poison. |
|---|---|---|---|---|---|
| Phosphorus ... | 1·23 | 1·00 | Antimony ... | 1·29 | 1·05 |
| Arsenic ......... | 1·23 | 1·00 | Bismuth ...... | 1·59 | 1·29 |

University of Bristol. [*Received, April 20th*, 1938.]

# 164. *A Comparison of the Rates of Hydrolysis of Methyl, Ethyl,* iso*Propyl, and* tert.*-Butyl Bromides in Acetone: Water Catalysis in Such Reactions.*

By William Taylor.

From the observed rates of hydrolysis, *viz.*, Me > Et < $Pr^{\beta}$ <<< $Bu^{\gamma}$, for this series of bromides in acetone containing "5%" and "10%" of water, support is given to a hydrolysis mechanism ($S_m$) previously proposed (J., 1937, 1965).

Further, the suggestion is made that the catalytic effect of water in such reactions

is due to its dissociating effect on the water already in solution in an organic solvent. A similar explanation is given to interpret the accelerating effect of water on the alcoholysis and acidolysis of alkyl halides.

THE hydrolysis of *tert.*-butyl bromide in acetone containing small concentrations of water is kinetically a second-order reaction. Hence, although the hydrolysis, under these conditions, cannot take place through a unimolecular mechanism, a bimolecular mechanism may be assumed (J., 1937, 1965). Since such solvents are presumably of low ionising power, according to the theory of Hughes and Ingold (J., 1935, 244; see also Hughes, *Trans. Faraday Soc.*, 1938, **34**, 198) a bimolecular mechanism might conceivably have been anticipated. From this viewpoint, then, there is no disagreement between their theory and experiment. However, further experimental evidence given here is widely divergent from what would be expected from their general theory of the hydrolysis of alkyl halides.

If it is accepted that the hydrolysis of *tert.*-bntyl bromide under these conditions is bimolecular, then the hydrolyses of methyl, ethyl, and *iso*propyl bromides under the same conditions are most probably also bimolecular. In this case, according to these authors (see also Hughes, *loc. cit.*), the second-order hydrolysis velocity coefficients should be $Me > Et > Pr^{\beta} > Bu^{\gamma}$. The purpose of this investigation was to discover whether or not the coefficients vary in this manner. As shown in Table I they do not, but are in fact $Me > Et < Pr^{\beta} \lll Bu^{\gamma}$.

A similar result (J., 1937, 992), found for the first-order hydrolysis velocity coefficients of the same series of bromides in "60%" and "80%" aqueous ethyl alcohol, has previously been attributed to a break in the reaction mechanism from bimolecular for methyl and ethyl bromides to unimolecular for *iso*propyl and *tert.*-butyl bromides (Bateman and Hughes, J., 1937, 1187). Because this supposed break in reaction mechanism cannot now be considered as the correct interpretation of the similar variation in the hydrolysis rates in "5%" and "10%" aqueous acetone, it is more than possible that the same conclusion holds good for aqueous ethyl alcohol.

An alternative scheme (J., 1937, 1965) is, however, capable of interpreting these results satisfactorily. According to this, all hydrolyses of alkyl halides are bimolecular, and the minimum at Et is held to be due to the decreasing facility of attack of $\alpha$-carbon by the hydroxyl of the reagent water molecule, together with the concurrently increasing facility of attack of the halogen (of the alkyl halide) by hydrogen of the water, down the series Me, Et, $Pr^{\beta}$, $Bu^{\gamma}$.

TABLE I.

*Values of the second-order velocity coefficients (expressed as l. g.-mol.$^{-1}$ hr.$^{-1}$ $\times$ $10^5$), for approximately half-reaction, in acetone at 50°.*

| G. of $H_2O$ in 100 c.c. of solution. | MeBr. | EtBr. | $Pr^{\beta}$Br. | $Bu^{\gamma}$Br.* |
|---|---|---|---|---|
| 5 | 9·84 | 3·02 | 4·81 | 5,990 |
| 10 | 16·5 | 5·22 | 7·30 | 18,400 |

* From J., 1937, 1855.

As noted previously (J., 1937, 1855), water is again seen to have an accelerating effect on its own reaction with an alkyl halide in acetone. Similarly, small concentrations of water accelerate the alcoholysis of benzhydryl chloride in ethyl alcohol (Farinacci and Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 2542) and also the acidolysis of $\alpha$-phenylethyl chloride in acetic acid (Steigman and Hammett, *ibid.*, p. 2539). On the other hand, nitrobenzene retards the alcoholysis of benzhydryl chloride (Farinacci and Hammett, *loc. cit.*). It is now suggested that these catalytic effects are due, not to the ionising effect of water on the alkyl halide (cf. the solvent theory of Hughes and Ingold), but to the dissociating effect of water, and to the associating effect of nitrobenzene, on the hydroxylic reagent R·OH, where R may be H, Alkyl, or Acyl, *i.e.*,

$$(R{\cdot}OH)_n \underset{(PhNO_2)\,(COMe_2)}{\overset{(H_2O)}{\rightleftarrows}} n\,ROH$$

The associated form of the reagent is assumed to be relatively unreactive compared with the simple form towards any alkyl halide. On this basis, in computing the second-order velocity coefficients, the active mass of the hydroxylic reagent should be that of the simple molecule, and constant values might then be expected under conditions which vary not too widely.

This interpretation is offered only to account for the catalytic influence of water and of organic solvents such as nitrobenzene and acetone. An explanation of the different rates of elimination of halogen from alkyl halides by different hydroxylic reagents such as water and ethyl alcohol has already been given (J., 1937, 1966) and is distinct from the above.

## EXPERIMENTAL.

The methyl, ethyl, and *iso*propyl bromides were materials of constant b. p. The acetone was "AnalaR," purified by the method of Conant and Kirner (*J. Amer. Chem. Soc.*, 1924, **46**, 246). The procedure in the kinetic experiments was as for *tert.*-butyl bromide (J., 1937, 1855), the temperature again being 50°. Acetone containing 5 g. and 10 g. of water in 100 c.c. of solution at 50° was employed, since no correction due to removal of hydrogen bromide was necessary (see *ibid.*) and also since, the conditions employed for *tert.*-butyl bromide being adhered to, water of this concentration gave measurable rates of development of acidity. The second-order coefficients were calculated from the equation

$$k = [2{\cdot}303/t(a - b)] \log_{10}[b(a - x)/a(b - x)]$$

$t$ being the time in hours, and $a$ and $b$ the ordinary concentrations (in g.-mol./l.) of water and the alkyl bromide respectively.

Details of representative individual runs are given in Table II, a summary of the results having been given in Table I.

### TABLE II.

*Methyl bromide.*

$a = 5{\cdot}5556$; $b = 0{\cdot}2148$.

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| $t$ | 171 | 268 | 432 | 576 | 746 | 840 | 1008 | 1175 | 1344 |
| $x$ | 0·0300 | 0·0452 | 0·0720 | 0·0914 | 0·1080 | 0·1176 | 0·1302 | 0·1366 | 0·1464 |
| $k \times 10^5$ | 15·9 | 15·9 | 17·1 | 17·5 | 16·5 | 17·2 | 16·9 | 15·7 | 15·6 |

*Ethyl bromide.*

$a = 5{\cdot}5556$; $b = 0{\cdot}1959$.

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $t$ | 381 | 572 | 716 | 885 | 980 | 1148 | 1315 | 1485 |
| $x$ | 0·0204 | 0·0294 | 0·0370 | 0·0448 | 0·0496 | 0·0560 | 0·0630 | 0·0666 |
| $k \times 10^5$ | 5·18 | 5·11 | 5·27 | 5·30 | 5·38 | 5·30 | 5·34 | 5·06 |

iso*Propyl bromide.*

$a = 5{\cdot}5556$; $b = 0{\cdot}0783$.

| | | | | | |
|---|---|---|---|---|---|
| $t$ | 522 | 762 | 1097 | 1265 | 1435 |
| $x$ | 0·0142 | 0·0200 | 0·0296 | 0·0310 | 0·0356 |
| $k \times 10^5$ | 6·90 | 6·98 | 7·81 | 7·18 | 7·62 |

In all experiments the dark colour, which was previously observed during the experiments on *tert.*-butyl bromide, developed. From work on olefin formation with these bromides (J., 1937, 1962) it may be assumed that only the substitution reaction ($S_m$), and no olefin reaction ($O_m$), occurs.

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# 165. *Decomposition Reactions of the Aromatic Diazo-compounds. Part IV. A New Synthesis of Aromatic Antimony Compounds.*

By F. B. Makin and William A. Waters.

The reactions described in Part II (J., 1937, 2007) have been applied to substituted benzenediazonium chlorides. Mixtures containing triarylstibine dichlorides, $Ar_3SbCl_2$, triarylstibines, $Ar_3Sb$, and diarylstibnous chlorides, $Ar_2SbCl$, are formed when solid diazonium chlorides react with metallic antimony under acetone or ethyl acetate, kept neutral with chalk. Under other solvents, such as water, ethyl alcohol, *cyclo*hexane, benzene, carbon tetrachloride, carbon disulphide, diethyl ether, and dioxan, the reaction does not occur, and it is inferred that diazonium chlorides react with antimony only after tautomeric change has occurred to the wholly covalent form Ar·N:NCl.

The similarity between this reaction and those of Nesmejanov and his colleagues (*Ber.*, 1929, **62**, 1010; 1935, **68**, 1877) has been demonstrated; *e.g.*, both the antimony and the zinc double diazonium chlorides can be used for the preparation of aromatic antimonials by this new reaction, which gives the organometallic compounds in very good yields. Diazonium chlorides seem to be able to chlorinate ethyl acetate as well as acetone.

It was reported in Part II (J., 1937, 2007) that phenylmercuric chloride and triphenylstibine dichloride were formed in appreciable quantities when benzenediazonium chloride was allowed to react, under acetone kept neutral with chalk, with mercury and antimony respectively. Both these syntheses of organometallic compounds have now been investigated more fully, with use of substituted benzenediazonium chlorides, and appear to be general reactions.

Particular attention has been paid to the reaction of diazonium chlorides with metallic antimony, and the earlier surmise (J., 1937, 2013) of the complexity of the reaction has been confirmed. Aromatic antimony compounds of three types, (*a*) triarylstibine dichlorides, $Ar_3SbCl_2$, (*b*) triarylstibines, $Ar_3Sb$, and (*c*) diarylstibnous chlorides, $Ar_2SbCl$, have been isolated as primary products in addition to antimony trichloride. Solid diazonium chlorides do not decompose spontaneously under acetone at room temperature, but immediately powdered antimony is added reaction sets in and much heat is evolved. The aromatic antimony compounds are obtained in the best yields when the mixture is kept neutral with chalk and cooled externally, for then the slower general reaction between a diazonium chloride and acetone, $Ar{\cdot}N_2Cl + CH_3{\cdot}CO{\cdot}CH_3 = N_2 + ArH + CH_2Cl{\cdot}CO{\cdot}CH_3$ (A), which requires a higher temperature for initiation, is almost entirely excluded.

Under ethyl acetate also diazonium chlorides react fairly rapidly with metallic antimony, with formation, in good yield, of a similar mixture of aromatic antimony compounds. Under a number of other solvents, however, no reaction occurs until the mixture is heated to the self-decomposition temperature of the diazonium chloride; a small amount of antimony trichloride but no aromatic antimony compounds then seem to be formed. Solvents useless for the synthesis of aromatic antimony compounds by this new reaction are water and ethyl alcohol, which dissolve and dissociate diazonium chlorides, and also *cyclo*hexane, benzene, carbon tetrachloride, carbon disulphide, diethyl ether, and dioxan, in all of which diazonium chlorides are insoluble.

From the complete absence of any action in water or alcohol it is evident that diazonium kations do not react with antimony, or with other metals with the possible exceptions of copper (in Gattermann's reaction) and mercury (in the reaction of McClure and Lowy, *J. Amer. Chem. Soc.*, 1931, **53**, 319). It has already been pointed out that the occurrence of reaction between diazonium chlorides and metals such as antimony, bismuth, lead, silver and tin (amongst others), in the presence of acetone, is most simply explained by supposing that diazonium chlorides, $(ArN_2)^+Cl^-$, can undergo tautomeric change to the wholly covalent, unstable diazo-form, Ar·N=NCl, which then loses nitrogen with production of transient free neutral radicals. The new experimental fact that aromatic antimony compounds of different structural types are produced simultaneously in this reaction is in full accord with this theory, for neutral aryl radicals and chlorine atoms would be expected to combine

independently of each other with any available substance containing an uncompleted electronic shell.

The occurrence of this reaction of diazonium chlorides under acetone and ethyl acetate, but not under the other organic solvents enumerated above, is remarkable. The authors suggest tentatively that the necessary condition for occurrence of any reaction between a diazonium salt and a metal is the presence of a solvent which is able somehow to promote the tautomeric change mentioned above. Metals themselves too must be catalysts for this change or for the subsequent decomposition of the covalent diazo-chloride, since, in the absence of a metal, no reaction occurs in the cold with acetone or ethyl acetate. The hypothesis that copper is an effective catalyst for the tautomeric change of a diazonium halide molecule to an unstable diazo-halide would explain its function in the well-known reactions of Gattermann.

Acetone and ethyl acetate may perhaps be effective catalysts for the tautomeric change of the diazonium chlorides in virtue of their highly polar character. It happens that nearly all the other solvents examined as yet have been non-polar liqnids, although they have widely differing chemical characters. Alternatively, acetone and ethyl acetate may promote the tautomeric change of diazonium salt molecules by dissolving slightly the isomeric non-ionic form, for obviously the chance of a reaction occurring between two solid powders (*e.g.*, benzenediazonium chloride and antimony under *cyclo*hexane, which dissolves neither) is much less than that of reaction between one solid and a solute with which it can get into intimate contact.

An examination of the decomposition of diazonium chlorides under ethyl acetate has shown that there is a similarity between this solvent and acetone, for both seem to be chlorinated by diazonium chlorides. When a mixture of a diazonium chloride and ethyl acetate is not kept neutral by addition of chalk, hydrogen chloride is formed on warming and an aryl chloride is produced; *e.g.*, benzenediazonium chloride yields some chlorobenzene (Part II) and *p*-chlorobenzenediazonium chloride yields some *p*-dichlorobenzene. When, however, the decomposition is carried out in the presence of an excess of chalk, a considerable quantity of acetaldehyde is formed. This may well result from chlorination of the ethyl acetate with production of the easily hydrolysed substance α-chloroethyl acetate, the reaction $Cl\cdot + CH_3{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}CH_3 \longrightarrow CH_3{\cdot}CHCl{\cdot}O{\cdot}CO{\cdot}CH_3$ (B) being exactly analogous to the chlorination of acetone (A).

Although the decomposition of simple aryldiazonium salts under acetone and ethyl acetate in the presence of metals has not been utilised previously for the preparation of their organometallic compounds, several reactions of very similar type have been described by Nesmejanov and his colleagues (*Ber.*, 1929, **62**, 1010, 1018; 1935, **68**, 1877; *J. Gen. Chem. Russ.*, 1936, **6**, 144, 167; *Sci. Rep. Moscow State Univ.*, 1934, No. 3, 291; see *Brit. Chem. Abstr.*, 1936, *A*, 837, 1004; 1937, *A*, ii, 282), who have worked with double salts of diazonium chlorides and the chlorides of the heavy metals mercury, tin, and lead. On decomposition with metals such as copper and tin (amongst others) these double salts, which can be prepared from aqueous solutions, yield arylmercuric chlorides or mercurydiaryls, diaryltin dichlorides, $Ar_2SnCl_2$, and triaryl-lead chlorides, $Ar_3PbCl$, respectively. Further, Dunker, Starkey, and Jenkins (*J. Amer. Chem. Soc.*, 1936, **58**, 2309) have reported that mixtures of diazonium borofluorides with mercuric chloride can be reduced under acetone with stannous chloride and yield arylmercuric chlorides in good yield. Nesmejanov (see *Brit. Chem. Abstr.*, 1937, *A*, ii, 282) seems to favour the view that the metal forming the organometallic compound is derived from the double chloride and need not be present as the free metallic element, although this may sometimes be formed during the reaction by a displacement process. However, if one adopts the hypothesis that neutral radicals are produced as the diazo-compound decomposes, one would expect these aryl radicals to attack, in the first instance, the free metal and not a stable metallic kation. Of course the organometallic compounds thereby produced might subsequently react with the metallic chloride to yield a more stable organometallic compound (compare Challenger and Ridgway, J., 1922, **121**, 107).

The latter hypothesis receives strong support from the present work with metallic antimony, for the double salt decomposition method of Nesmejanov is also a satisfactory

procedure for the production of aromatic antimony compounds. Both the double antimony salts of the type $ArN_2Cl,SbCl_3$ described by May (J., 1912, **101**, 1037) and also the better known double zinc diazonium chlorides can be decomposed under acetone with antimony and yield a mixture of organic antimony compounds exactly similar to that obtained with the simple diazonium chlorides, which are so much more difficult to prepare in the solid state. The best yields of aromatic antimony compounds have been obtained by using the double zinc diazonium chloride precipitated from an aqueous solution of ar aromatic amine after its diazotisation with sodium nitrite in the usual way.

The products were best isolated from the acetone or ethyl acetate solutions by evaporating the solvent and extracting the residue with light petroleum or benzene. The triarylstibine dichlorides and the diarylstibnous chlorides were identified, after isolation, by quantitative hydrolysis with alcoholic potash and estimation of the liberated chloride ions Both the triarylstibines and the diarylstibnous chlorides were established as being compounds of tervalent antimony by addition of chlorine in carbon tetrachloride solution. Further, the aromatic amines used—*p*-chloroaniline, *p*-bromoaniline, 4-chloro-*o*-toluidine, 5-chloro-*o*-toluidine, and 4-chloro-*o*-anisidine—although primarily chosen on the advice of Mr. K. H. Saunders for their ease of formation of pure diazonium chlorides, all contained halogen atoms as nuclear substituents, and estimation of the total halogen content of their organometallic products gave valuable confirmatory evidence of structure. From aniline, *p*-chloroaniline, and *p*-bromoaniline, the chief products were the triarylstibine dichlorides, but from the other bases, which contained *o*-substituents, only traces of quinquevalent antimony compounds were formed, the chief prodncts being the triarylstibines accompanied by a smaller quantity of the diarylstibnous chlorides. This difference in the nature of the products may perhaps be due to steric hindrance, and, in accordance with this view, it was noticed that the substituted triarylstibines which were obtained did not react rapidly with halogens.

## EXPERIMENTAL.

The substituted diazonium chlorides were prepared by diazotising, with amyl nitrite, a suspension of the dry hydrochloride of the requisite base in absolute alcoholic hydrogen chloride at 0—10° and treating the resulting clear solution with anhydrous ether (compare Knoevenagel, *Ber.*, 1890, **23**, 2995). With the exception of the salt obtained from 4-chloro-*o*-toluidine, the diazonium chlorides were strongly hygroscopic. They were thoroughly washed with the solvent to be employed and then used immediately.

*Reactions of Substituted Diazonium Chlorides with Acetone.*—(i) *Decomposition in absence of chalk.* 20 G. of *p*-chlorobenzenediazonium chloride were covered with 100 c.c. of acetone. No reaction occurred in the cold, but at 50° nitrogen and hydrogen chloride were evolved. On fractionation the resulting mixture yielded 1 g. of pure chlorobenzene and 3 g. of chloroacetone (semicarbazone, m. p. 147·5°).

(ii) *Decomposition in presence of chalk.* The same quantities were used together with 20 g. of precipitated chalk. The product gave 1·5 g. of chlorobenzene and 6 g. of chloroacetone. *p*-Dichlorobenzene was not detected in either experiment.

*p*-Bromobenzenediazonium chloride (from 26 g. of the amine hydrochloride), decomposed in acetone containing chalk, gave 10·5 g. of chloroacetone and 7·9 g. of bromobenzene (identified by conversion into *p*-bromonitrobenzene, m. p. and mixed m. p. 126°).

(iii) *Decomposition in presence of lead, silver, and bismuth.* To separate portions of 5 g. of *p*-chlorobenzenediazonium chloride under 100 g. of acetone containing 5 g. of chalk were added (a) 20 g. of lead filings, (b) 5 g. of silver powder, and (c) 10 g. of precipitated bismuth. In each case reaction set in in the cold, and was completed by refluxing for ½ hour. After cooling, each solution was filtered. The residue from (a) was extracted with hot water, but no lead chloride was removed. However, a solution containing lead ions in quantity was obtained by warming the insoluble residue with dilute acetic acid and filtering.

The residue from (b) was extracted with warm dilute aqueous ammonia; the filtered extract gave, on acidification with nitric acid, 1·3 g. of silver chloride.

The residne from (c) was extracted with warm dilute acetic acid, but did not yield a solution containing bismuth ions. The acetone solution, however, when evaporated, left a tarry residue which, on extraction with dilute hydrochloric acid, gave a solution containing bismuth ions in quantity.

(iv) *Reaction with mercury.* 15 G. of *p*-chlorobenzenediazonium chloride were shaken under

100 c.c. of acetone with 30 g. of mercury and 20 g. of chalk and the reaction was completed by warming for ½ hour. After cooling, the solid was removed by filtration and found to contain both mercurous and mercuric salts. The filtrate on evaporation yielded 1·5 g. of *p*-chlorophenylmercuric chloride, m. p. 241° (Found : Hg, 57·7; total Cl, 20·4. Calc. : Hg, 57·6; total Cl, 20·4%). Hanke (*J. Amer. Chem. Soc.*, 1923, **45**, 1321) gives m. p. 225°, and Nesmejanov (*Ber.*, 1929, **62**, 1010) m. p. 240°.

From *p*-bromobenzenediazonium chloride, 0·8 g. of *p*-bromophenylmercuric chloride, m. p. 248°, was obtained by a similar method.

*Reactions of Diazonium Chlorides with Ethyl Acetate.*—(i) *Decomposition in presence of chalk.* 20 G. of *p*-chlorobenzenediazonium chloride were added to 200 c.c. of purified ethyl acetate and 20 g. of chalk. Reaction set in at 60° and the mixture became red. After refluxing for ½ hour, the mixture was cooled, and the filtered liquid fractionated. The ethyl acetate fraction, b. p. 75—80°, contained acetaldehyde in sufficient quantity for the preparation of its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 161°. A small quantity of yellowish oil, distilling between 100° and 160°, contained hydrolysable chlorine and had an acidic reaction. No chlorobenzene, however, was detected. The remainder was distilled under reduced pressure and yielded 0·4 g. of pure *p*-dichlorobenzene, m. p. and mixed m. p. 53·5°.

(ii) *Decomposition in presence of lead, silver, and bismuth.* To separate portions of *p*-chlorobenzenediazonium chloride in ethyl acetate containing chalk were added powdered lead, silver, and bismuth. In each case reaction set in in the cold and was completed by refluxing, some acetaldehyde being evolved. The solutions were then cooled and filtered. The residue from the reaction with lead was extracted with hot water; the extract yielded lead chloride. The filtrate from this reaction, when distilled, gave a fraction, b. p. 100—125°, containing acetaldehyde and hydrogen chloride.

The residue from the reaction with silver was extracted with warm dilute aqueous ammonia; the extract on acidification gave silver chloride. The filtrate from this reaction, on fractionation, gave a portion, b. p. 100—145°, acid to litmus, containing acetaldehyde, hydrogen chloride and acetic acid. The filtrate from the reaction with bismuth deposited bismuth oxychloride on evaporation.

*The Influence of Solvents on the Reaction of Benzenediazonium Chloride with Metallic Antimony.*—(i) *Acetone.* A simpler method for isolating the reaction product, $Ph_3SbCl_2$, than that described in Part II was to evaporate the acetone solution to dryness and extract the residue with light petroleum (b. p. 60—80°). This established that the triphenylstibine dichloride was a primary reaction product. No other aromatic antimony compounds were isolated.

(ii) *Water.* 0·2 G.-mol. of aniline was diazotised in 300 c.c. of 3N-hydrochloric acid at 0° and 20 g. of antimony powder were then added to the vigorously stirred liquid. The antimony did not react and, after warming, only phenol was obtained.

(iii) 6 G. of benzenediazonium chloride, 5 g. of sieved antimony powder, and 5 g. of chalk were mixed under 50 g. of absolute ethyl alcohol. There was no reaction in the cold, but, on warming, acetaldehyde was evolved. After cooling, the liquid was filtered; it did not contain any aromatic antimony compound.

The above experiment was repeated with *cyclo*hexane, benzene, carbon tetrachloride, carbon disulphide, diethyl ether, and dioxan. In no case did any reaction occur in the cold. After decomposition by heat (except in the case of the ether mixture, which could be refluxed without change) a tarry mass resulted, from which traces of inorganic antimony compounds but no aromatic antimony compounds could be isolated. When carbon disulphide was used, a little diphenyl disulphide was formed (compare Parts I and III).

*Preparations of Organic Antimony Compounds from Substituted Benzenediazonium Chlorides.*—(i) 20 G. of *p*-chloroaniline hydrochloride were converted into the solid diazonium chloride, which was then mixed with 20 g. of chalk and 200 c.c. of acetone. On addition of 30 g. of antimony powder a vigorous reaction ensued and the acetone boiled. After reaction had subsided, the mixture was refluxed for ½ hour, filtered hot, and the residue extracted with more warm acetone. The filtrate was evaporated to dryness, and the residue extracted with light petroleum (b. p. 60—80°). On cooling, colourless needles of *tri*-p-*chlorophenylstibine dichloride* (1·4 g.) separated, m. p. 193° (Found : Sb, 23·0; hydrolysable Cl, 13·4. $C_{18}H_{12}Cl_5Sb$ requires Sb, 23·1; hydrolysable Cl, 13·4%).

When ethyl acetate was used as the solvent, the reaction was not so vigorous, but the same product was isolated in an identical yield.

(ii) The diazonium salt from *p*-bromoaniline hydrochloride (26 g.) reacted similarly in each solvent. In ethyl acetate, *tri*-p-*bromophenylstibine dichloride* (4·1 g.), m. p. 200°, was obtained;

in acetone the yield was 3·0 g. (Found: Sb, 18·5; hydrolysable Cl, 10·3. $C_{18}H_{12}Cl_2Br_3Sb$ requires Sb, 18·3; hydrolysable Cl, 10·7%).

(iii) The solid diazonium chloride from 4-chloro-*o*-toluidine hydrochloride (20 g.) was allowed to react, in the cold, with antimony powder in acetone containing chalk. After refluxing, the solid residue was thoroughly extracted with acetone; when the combined extracts were evaporated, *tri-(4-chloro-o-tolyl)stibine* (6·1 g.) separated, which crystallised from benzene in long matted needles, m. p. 226° (Found: Sb, 24·4; total Cl, 21·5; hydrolysable Cl, 0. $C_{21}H_{18}Cl_3Sb$ requires Sb, 24·4; total Cl, 21·4%).

When ethyl acetate was used as the solvent, tri-(4-chloro-*o*-tolyl)stibine (5·6 g.) was obtained and also a small quantity of the more soluble di-(4-chloro-*o*-tolyl)stibnous chloride (see below).

(iv) The diazonium chloride from 5-chloro-*o*-toluidine reacted similarly to its isomer. The products were crystallised first from ethyl acetate containing alcohol and finally from light petroleum. *Tri-(5-chloro-o-tolyl)stibine*, which formed fine needles, m. p. 176°, was obtained both with acetone and with ethyl acetate (Found: Sb, 24·45; total Cl, 21·5; hydrolysable Cl, 0. $C_{21}H_{18}Cl_3Sb$ requires Sb, 24·4; total Cl, 21·4%). From the ethyl acetate reaction there was isolated also a small quantity of *tri-(5-chloro-o-tolyl)stibine dichloride*. This was also prepared by treating the corresponding stibine with chlorine in carbon tetrachloride solution. It crystallised from light petroleum in prisms, m. p. 238° (Found: Sb, 21·5. $C_{21}H_{18}Cl_5Sb$ requires Sb, 21·4%).

(v) Similar reactions were carried out, acetone and ethyl acetate being used, with the diazonium salt from 4-chloro-*o*-anisidine hydrochloride. After removal of the solvents, the products were washed with dilute hydrochloric acid and with methyl alcohol to remove antimony chloride and tar, and then crystallised successively from ethyl acetate, alcohol, and light petroleum. From the reaction in acetone there was obtained *di-(5-chloro-2-methoxyphenyl)stibnous chloride*, m. p. 144° (Found: Sb, 27·3; hydrolysable Cl, 8·1. $C_{14}H_{12}O_2Cl_3Sb$ requires Sb, 27·0; hydrolysable Cl, 8·05%). It reacted slowly with solutions of chlorine and bromine in carbon tetrachloride.

From the reaction in ethyl acetate there were obtained *tri-(5-chloro-2-methoxyphenyl)stibine*, m. p. 188° (Found: Sb, 22·2; hydrolysable Cl, 0. $C_{21}H_{18}O_3Cl_3Sb$ requires Sb, 22·2%), and also a little *tri-(5-chloro-2-methoxyphenyl)stibine dichloride*, m. p. 281° (decomp.) (Found: Sb, 19·7. $C_{21}H_{18}O_3Cl_5Sb$ requires Sb, 19·7%). The latter compound was also obtained by treating the corresponding stibine with chlorine in carbon tetrachloride solution.

*Use of the Antimony Chloride Double Salt.*—From 20 g. of aniline, May's double salt of benzenediazonium chloride and antimony chloride was prepared from aqueous solution, washed with acetone, and added to 30 g. of antimony powder and 20 g. of chalk in 200 c.c. of acetone cooled in ice. After the vigorous reaction had subsided, the mixture was refluxed for ½ hour, and the filtered liquid evaporated. The residue was crystallised from alcohol containing some hydrochloric acid and yielded 3·5 g. of triphenylstibine dichloride, m. p. 143°.

*Use of Zinc Chloride Double Salts.*—(i) 20 G. of aniline were diazotised in aqueous solution (100 c.c.) and the crystalline double zinc diazonium chloride was precipitated by the addition of a concentrated solution of zinc chloride. This was washed with acetone and added to antimony and chalk under acetone. After the reaction had subsided, the mixture was refluxed for ½ hour and cooled; after filtration, the residue was washed with more acetone. The acetone soluwas evaporated, and the residue redissolved in alcohol containing some hydrochloric acid; on cooling, triphenylstibine dichloride (8·5 g.) separated.

(ii) 40 G. of 4-chloro-*o*-toluidine hydrochloride were diazotised in 100 c.c. of 3N-hydrochloric acid and the filtered diazonium salt solution was added to a concentrated solution of zinc chloride. The precipitated double salt was collected, washed with acetone, and added to 40 g. of antimony powder and 30 g. of chalk in 250 c.c. of acetone. Reaction was completed by refluxing for ½ hour. After cooling, the liquid was filtered, and the residue washed with cold acetone. The acetone solution was evaporated to dryness, leaving a residue, which was extracted first with light petroleum and then with benzene. From the petroleum solution 7 g. of *di-(4-chloro-o-tolyl)stibnous chloride*, m. p. 131°, were obtained (Found: Sb, 29·8; hydrolysable Cl, 8·9. $C_{14}H_{12}Cl_3Sb$ requires Sb, 29·8; hydrolysable Cl, 8·7%). This slowly decolorised bromine in carbon tetrachloride solution; with chlorine in carbon tetrachloride solution it yielded *di-(4-chloro-o-tolyl)stibnic trichloride*, m. p. 162° (Found: Sb, 25·5. $C_{14}H_{12}Cl_5Sb$ requires Sb, 25·4%). From the benzene extract was isolated 0·2 g. of *tri-(4-chloro-o-tolyl)stibine dichloride*, m. p. 264° (Found: Sb, 21·1. $C_{21}H_{18}Cl_5Sb$ requires Sb, 21·4%). This was also obtained by treating the corresponding stibine with chlorine in warm carbon tetrachloride solution. It crystallised from carbon tetrachloride, but was sparingly soluble in petrol.

The residue containing the excess of antimony and the chalk was also extracted (Soxhlet) with acetone. 12 G. of tri-(4-chloro-*o*-tolyl)stibine, m. p. 226° (see above), were obtained.

A zinc chloride double salt could not be obtained from diazotised 5-chloro-*o*-toluidine.

The authors thank Mr. K. H. Saunders for advice in the choice of the diazonium chlorides used in these experiments and the Dyestuffs Group Research Committee of Imperial Chemical Industries Ltd. for the gift of the requisite aromatic amines. One of them (F. B. M.) also thanks the Education Committee of the Borough of West Hartlepool for a grant which has assisted him in participating in this work.

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## 166. *The Activation Energy of Organic Reactions. Part I. Electronic Theories of Organic Chemistry from the Standpoint of Chemical Kinetics.*

By C. N. Hinshelwood, K. J. Laidler, and E. W. Timm.

In this paper an attempt is made to correlate certain aspects of the electronic theory of organic reactions with the modern analysis of activation energy. The reactive centres in a molecule and in an attacking reagent are characterised *schematically* by effective charges which, according to sign, facilitate or oppose their mutual approach. Modification of the charges, by the introduction of substituents or by change of reagent, are thought of as adding algebraically extra classical electrostatic terms to the (largely non-classical) repulsion energies and to the bond energies involved in the energy of activation. Detailed consideration on this basis leads to the prediction of various regularities, which assist the interpretation of the experimental facts relating to the influence of substitution on reactivity.

The influence of substituent atoms on the reactivity of organic compounds can be interpreted in an illuminating way by the theory of internal electron displacements of the two types, inductive and electromeric, which was first advanced in a generalised form by Robinson between 1919 and 1926 and developed by him and by Ingold and others (Hamilton and Robinson, J., 1916, **109**, 1029; Robinson, *ibid.*, p. 1038; Robinson and Robinson, J., 1926, 2204; Kermack and Robinson, J., 1922, **121**, 433; Robinson, *J. Soc. Chem. Ind.*, 1925, **44**, 456, 563; Allan, Oxford, Robinson, and Smith, J., 1926, 402; Robinson, "Outline of an Electrochemical Theory of the Course of Organic Reactions," 1932; Ingold and Ingold, J., 1926, 1310; Ingold, *Chem. Reviews*, 1934, **15**, 225).

From a totally different point of view the subject can be treated in terms of the ordinary conceptions of reaction kinetics such as activation energies, collision numbers, and probability factors. The two ways of approach are largely independent, but there is a certain common ground where they overlap, and it is obviously desirable that the ideas used in each should be expressible in terms of one another. The present paper attempts to contribute to this clarification.

The treatment is a compromise between the purely non-physical approach of organic chemistry and the formally exact but complicated methods of the quantum-mechanical theory. The variations in certain *bond energies* and certain *interaction energies* between molecules are schematised by classical electrostatic terms. No attempt at application of rigid principles in calculating the energies is made, the main object being to show that certain interesting results follow from a consideration of the *balance* between the two *kinds* of energy terms referred to.

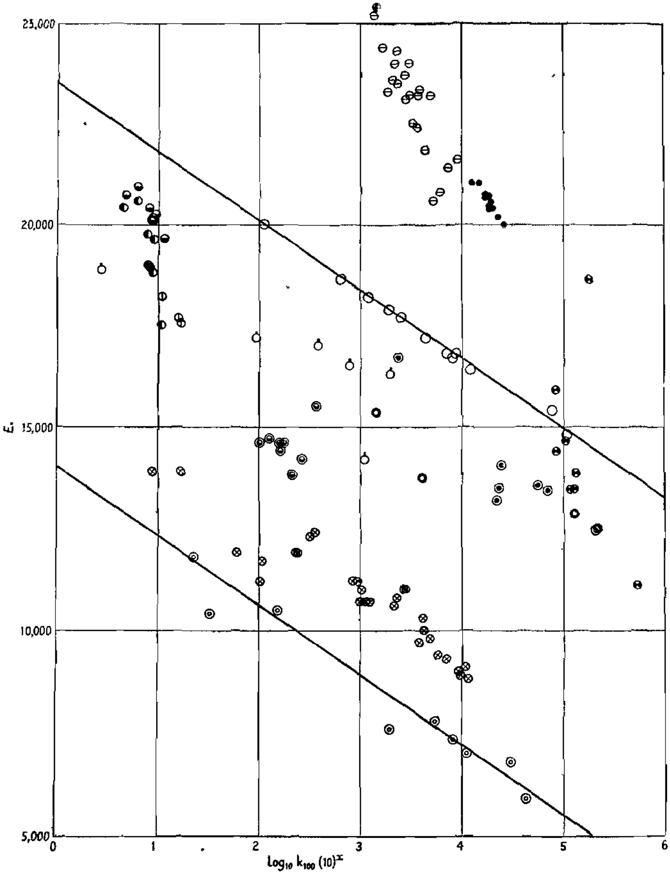
*Electronic Theories of Organic Reactivity.*—According to the modern theory, a substituent alters the reactivity of the parent compound by altering the availability of electrons at the point of reaction. According to Robinson, the total electronic effect may be divided into the general polar effect and the electromeric effect. The former is due to the unequal sharing of electrons between atoms, the latter to what is now called a resonance between possible electronic structures satisfying the octet rule. Both are permanent to a certain extent but also time-variable, especially the electromeric effect, the time-variability

depending upon the demands of the attacking reagent. The sign of the charge produced by the substituent may be inferred from physical considerations such as dipole moments (see, *e.g.*, Sutton, *Proc. Roy. Soc.*, 1931, **133**, *A*, 668). The effect of a series of substituents in a given reaction generally follows the order predicted from the sign and magnitude of the induced charges: apparent anomalies can be explained in terms of a finer analysis of the relative importance of the general polar and electromeric effects. Reactions have been classified as class A or class B according as the reaction is facilitated by accession of electrons to or recession of electrons from the point of attack (Ingold and Rothstein, J., 1928, 1217). This terminology is convenient in classifying data, but gives no insight into the actual mechanism. In particular, it is impossible to predict to which class the reaction belongs, as was clearly pointed out by Oxford and Robinson for the case of hydrolysis (J., 1926, 384). Ingold has also classified reactions into types $S_N1$ and $S_N2$ according to whether a unimolecular ionisation or a bimolecular interaction with a reagent determines the rate. Much of his discussion is helpful for the purpose of this paper, though the point of view is different.

The present paper suggests possible lines along which the problem may be approached from the point of view of the activation energy and the various terms of which it is made up.

*Reactivity and activation energy.* The rate of a chemical reaction may be represented by the equation $k = PZe^{-E/RT}$, where $E$ is the activation energy, $Z$ the collision number, and $P$ the probability that activated collisions shall result in reaction, being a measure of conditions other than activated collision which must be fulfilled. The order of magnitude of $Z$ does not vary, and the question arises whether the changes of reactivity with which the electron-drift theories deal depend chiefly upon changes in $E$ or upon changes in $P$. It now seems clear that changes in $E$ are of primary importance. Naturally, if the substituent which alters the reactivity of a parent substance is very close to the seat of reaction, as, *e.g.*, in the hydrolysis of substituted acetic esters, then steric effects may distort the picture to some extent; and such a series of compounds is not so suitable for study as a series of *m*- or *p*-substituted aromatic compounds, where purely electronic effects will be more clearly in evidence. Fig. 1 shows most of the available data for series where $E$ has been determined with reasonable accuracy. The method of representation is to plot $\log k_{100°}$ against $E$ for the reactions of a series. If changes in velocity from one reaction of the series to another are due to changes in $E$ alone, then the slope of the line is $-2{\cdot}303\boldsymbol{R}T$. If the line has a greater slope than this, then the value of $P$ is not constant for the series but increases with $E$. In the figure, $k_{100°}$ is multiplied by various powers of ten (indicated in the legend) to prevent confusion of the points belonging to different series. The following series may be said to show a constant value of $P$: halogenation of phenyl and tolyl ethers (Bradfield and Jones, J., 1928, 1006, 3073; 1931, 2903, 2907), benzoylation of amines (Williams and Hinshelwood, J., 1934, 1079), alkaline hydrolysis of benzoic esters (Ingold and Nathan, J., 1936, 222; Evans, Gordon, and Watson, J., 1937, 1430; Newling and Hinshelwood, J., 1936, 1357), alcoholysis of triarylmethyl chlorides (Nixon and Branch, *J. Amer. Chem. Soc.*, 1936, **58**, 492), reaction between substituted dimethylanilines and trinitroanisole (Hertel and Dressel, *Z. physikal. Chem.*, 1935, *B*, **29**, 178). In the esterification of benzoic esters the points are grouped too closely to allow a decision to be made. In the cases of acid hydrolysis of benzoic esters (Timm and Hinshelwood, Part III), alcoholysis of acyl chlorides (Branch and Nixon, *J. Amer. Chem. Soc.*, 1936, **58**, 2499), hydrolysis of arylsulphuric acids (Burkhardt, Horrex, and Jenkins, J., 1936, 1649), and the bromination of acetophenones (Evans, Morgan, and Watson, J., 1935, 17, 1167), $P$ tends to increase as $E$ increases. This effect is interesting but is of secondary importance, since for a series it is never large enough to outweigh changes in $E$. It has been explained tentatively on statistical principles as a general phenomenon which is to be expected when the average time required for a collision complex to complete its electronic rearrangements is large compared with the duration of a collision (Fairclough and Hinshelwood, J., 1937, 538). Whether this or another explanation is the correct one, there is little doubt that the phenomenon is due to a general cause not directly connected with the influence of substituents. According to the statistical theory referred to, the appearance or non-appearance

FIG. 1.




A ◎ *Benzoylation of amines; x = 4.*

B ○ *Alkaline hydrolysis of ethyl benzoates in* $C_2H_5{\cdot}OH{-}H_2O$ *solvent; x = 4.*

C ● *Alkaline hydrolysis of ethyl benzoates in* $CH_3{\cdot}CO{\cdot}CH_3{-}H_2O$ *solvent; x = 4.*

D ◉ *Alcoholysis of triarylmethyl chlorides; x = 3.*

E ♁ *Reaction between substituted dimethylanilines and trinitroanisole; x = 5.*

F ⊗ *Halogenation of phenyl and tolyl ethers;*

H ◐ *Acid hydrolysis of ethyl benzoates in* $C_2H_5{\cdot}OH{-}H_2O$ *solvent; x = 5.*

I ◒ *Acid hydrolysis of ethyl benzoates in* $CH_3{\cdot}CO{\cdot}CH_3{-}H_2O$ *solvent; x = 5.*

J ⦶ *Acid hydrolysis of methyl benzoates in* $CH_3{\cdot}OH{-}H_2O$ *solvent; x = 5.*

K ⊕ *Alcoholysis of acyl chlorides; x = 5.*

L ⊖ *Hydrolysis of arylsulphuric acids; x = 5; E − 3,000 is plotted as ordinate.*

M ● *Bromination of acetophenones;* k *in*

of the effect in a given series of reactions depends upon the exact time relations involved in the reaction mechanism.

The conclusion may, therefore, be reached that the changes of reactivity which result from electronic displacements caused by substituents are due primarily to changes in the activation energy.

*Factors determining the magnitude of activation energy.* In order to form a picture of how substituents may alter activation energy, we first consider how the activation energy is made up in a simple system such as A + BC = AB + C. According to the Heitler–London theory of the interaction of atoms and molecules, BC will repel A. This repulsion prevents the close approach of A, and preserves BC from reaction. For the mechanism of activation two extreme cases are imaginable : (1) A is forced up against the repulsion of BC until it is so close that it competes for B on equal terms with C, which is finally expelled. (2) BC is given so much energy that the bond between B and C is disrupted, after which A and B can combine without further opposition. As the calculations of Eyring and Polanyi showed (*Z. physikal. Chem.*, 1931, *B*, **12**, 279), it is usually more economical for the reaction to proceed by a compromise between these two mechanisms, A being forced up against the repulsion and the bond between B and C being stretched at the same time until A and C can compete on equal terms for B. Thus we can regard the activation energy as being made up of two parts : that required to overcome the repulsion of the approaching reagent, and that required to weaken the existing bond. In extreme cases one or the other of these might conceivably be the only factor. In practice we know, of course, that sometimes, though not usually, dissociation of one reactant is the controlling step in a reaction. The general case is represented in Fig. 2.

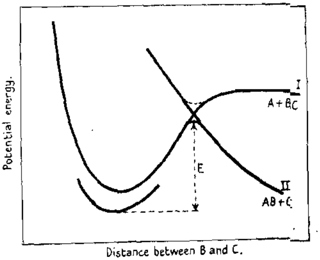
A B——$r_0$——C (normal)

A----------$r$----------B----------$r_1$----------C (activated)

Fig. 2.

From the point of view of an Eyring–Polanyi diagram, four energies come into consideration : (1) the bond strength of the link BC, (2) the repulsion between A and BC, (3) the repulsion between AB and C, and (4) the bond strength of the link AB which is formed. Fig. 3 shows an energy diagram, which consists of two curves (cf. Evans and Polanyi, *Trans. Faraday Soc.*, 1938, **34**, 11). Curve I is a normal attraction curve with a minimum for any given distance between A and BC. As the distance between A and BC becomes smaller, this curve shifts upward on the diagram. Curve II is the repulsion curve for AB and C. The intersection of the two curves, slightly rounded off owing to resonance between two states, corresponds to the energy of the activated state, and the energy of activation is given by the vertical distance between the minimum of the BC attraction curve when A is at infinity and the intersection.

Fig. 3.




Of the energies enumerated above, positive increments in (1), (2), and (3) increase $E$, that in (1) by deepening the depression in curve I at all separations between A and BC, that in (2) by raising curve I without affecting the curve for infinite separation of A and BC, and that in (3) by the vertical displacement of curve II. On the other hand, a positive increment in (4) lowers the activation energy by lowering curve II, since a higher bond strength results in a lower potential energy of the system AB + C. In the terminology of Evans and Polanyi, (1), (2), and (3) are sources of inertia, (4) of driving force.

For the purpose of discussing the changes in activation energy caused by substituents, we shall make the following assumption, which seems reasonable as an approximation, *viz.*, that the additional charges appearing on given atoms as a result of electron displacements introduce an extra electrostatic term into the energy of the bond between the given atom and its neighbour, and that this term can be calculated as though it were entirely a classical Coulombic one. Just as the change in charge caused by a substituent on an atom which is a reaction centre is assumed to add or to subtract an extra electrostatic term to or from the bond energy, so also it adds or subtracts one to or from the repulsion energy of an approaching reagent. The main parts of both energies are, in fact, non-classical, but the *variations* due to the substituents will be treated here as ordinary electrostatic terms. This simple scheme appears capable of explaining a number of facts.

We may first consider in a qualitative way the effect of a substituent in the part B of the molecule depicted in Fig. 2. Suppose B contains a carbon atom attached to an electron-attracting group, such as a nitro-group. This group is thought of as conferring on the carbon atom a positive charge $\delta e$ which is added algebraically to the charge which the atom bears in the unsubstituted compound. Suppose, for definiteness, that A is a negative ion and that C also is a negative centre. The positive charge added to B will therefore increase the strength of the bond BC. On the other hand, it will diminish the repulsion of the approaching A by superposing a Coulombic attraction on the normal force. In this way there are two opposing effects, one tending to increase and the other to decrease the activation energy. The bond strength of the product AB will be increased and the repulsive force between AB and C will be reduced. These factors also lower the activation energy. Thus there are three factors tending to lower the activation energy and one tending to raise it.

For our present purpose it is convenient, instead of considering all four terms separately, to consider the repulsion energy which must be overcome in bringing A up to the distance $r$ of the transition state, and energy which must be utilised in stretching BC from the length $r_0$ to $r_1$; $r$ and $r_1$ are functions of the four terms referred to above, but the regrouping into two terms will be convenient for an approximate treatment of the influence of substituents to be given later. We shall therefore speak of the activation energy as consisting of two parts: reagent repulsion energy, or simply *repulsion energy*, and *bond-stretching energy*.

In the light of this regrouping of the energy terms, we can say that in the example just considered the repulsive energy is lowered and the bond energy is increased. Conversely, an electron-repelling substituent will tend to decrease $E$ by weakening the bond, and to increase it by increasing the repulsion energy. Since we know that reactions may occasionally involve the preliminary dissociation of a reactant, we see that repulsion energy and bond energy must vary widely and either might be the determining factor. In general, since the relative importance of the two factors varies from reaction to reaction, we are faced with an ambiguity, and no further predictions can be made without more detailed investigation. It might be expected that generally the change in the strength of the existing bond will be the less important since this is counterbalanced by three opposing changes, but this is not certain. Robinson has emphasised the fact that in additions to unsaturated systems and in benzene substitution the course of events is governed by the ease of approach of a positive (kationoid) reagent to a centre of available electrons in the molecule attacked. In these cases, evidently, modifications of the repulsive energy are of primary importance. In other reactions it can be seen that the changes in bond strength determine the influence of substituents on the course.

The following simple considerations show how the ambiguity can be to some extent resolved. We assume effective charges $e_A$, $e_B$, and $e_C$ on A, B, and C respectively. The work done in bringing A up from infinity against the repulsion of BC to its position in the transition complex is given by

$$E_1 = W_1 - \int_{\infty}^{r} \frac{e_A e_B}{x^2} dx = W_1 + \frac{e_A e_B}{r} \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where the second term represents the electrostatic part with which we are primarily

concerned. Meanwhile, the charge on C has to be removed from the distance $r_0$ to the distance $r_1$, for which the work is given by

$$E_2 = W_2 - \int_{r_0}^{r_1} \frac{e_B e_C}{x^2} dx = W_2 - \frac{e_B e_C}{r_1}\left(\frac{r_1}{r_0} - 1\right) \quad . \quad . \quad . \quad . \quad . \quad (2)$$

In so far as the effect of the substituent on B can be schematised by a change $\delta e_B$ in $e_B$, then the corresponding changes in activation energy are

$$\Delta E_1 = e_A \delta e_B / r \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

and

$$\Delta E_2 = -\frac{e_C \delta e_B}{r_1}\left(\frac{r_1}{r_0} - 1\right) . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

These values are opposed to one another.

In an analogous way changes in $e_A$ or $e_C$ would yield similar formulæ.

The bond BC is mainly covalent, and consequently will be disrupted by a relatively small extension. The activation energy is a small fraction only of the bond strength. *In general, therefore,* $r_1/r_0$ *will not exceed unity very greatly*, and will probably be much less than 2; $r_1$ and $r$ being of the same order of magnitude, it follows that for equal values of $e_B$ and $e_C$, $\Delta E_2$ will be less than $\Delta E_1$. Thus the influence of the substituent on the activation energy will follow its influence on the repulsion of the reagent which approaches the active centre. This conclusion confirms that reached above from the consideration of the four energy terms. By considering how the various factors in these equations change as changes in the reactants are made, it is possible to arrive at various conclusions, of which the three following appear to be the most important. It must here be clearly stated that we are faced with two problems: that of determining the relative average magnitudes of the activation energies when comparing one reaction type with another, and that of determining the relative importance of the repulsion and bond energies when substituents are altered in either reactant. As will be seen, however, similar considerations can be applied in the solution of both problems.

As our first conclusion we re-state that arrived at above:

I. *There should be a general tendency for the influence of the substituent on the activation energy to follow the direction indicated by its effect on the attraction of the reagent to the seat of reaction.*

When, however, $e_A$ becomes small, the relative importance of $\Delta E_1$ diminishes, and finally $\Delta E_2$ may predominate. We thus arrive at the second conclusion:

II. *The tendency referred to in* I *will weaken with the weakening or removal of any well-defined positive or negative centre in the attacking reagent. When such a centre has become weak enough, there will be a reversal of the effect, and the influence of the substituent will now be determined by its effect on the bond energy.*

A variation of this rule predicts the effect of changes in the charge of the central atom itself.

Another case in which a trend in this same sense occurs may be foreseen by considering the distances $r$ and $r_1$. Most of the repulsive energy and most of the bond energy consists of parts which are (in our approximation) permanent and unchanged by the substituent, and these will vary greatly with change of the reagent A or of the molecule BC to be disrupted. Suppose we change from a given attacking reagent to another, the permanent repulsion of which by BC is much greater. Activation being a compromise between the two processes of forcing up the reagent and stretching the bond, the most economical reaction route will now be that involving a greater stretching of BC and a less intimate approach of A. Thus $r_1$ becomes greater *and* $r$ greater. In the limit of extreme repulsion, the most economical mode of reaction would be by the complete disruption of BC. As we move in the direction of this limiting case the relative importance of the repulsion energy diminishes and that of the bond energy increases. This is reflected in an increase of $\Delta E_2/\Delta E_1$ as $r$ and $r_1$ increase, the charges being assumed to remain the same. Thus we arrive at another principle.

III. *If the same molecule is attacked by two different reagents whose charges do not differ greatly, then as the total activation energy increases, it is influenced by substituents in the attacked molecule less and less in the sense predicted from the change in the repulsion of the reagent and may, for very large activation energies, become subject to influences parallel with those of the substituent on the bond strength.*

A converse rule can obviously be deduced for the case of the same reagent attacking different molecules of the type BC.

The above generalisations do not allow absolute predictions to be made; but starting from I—which is of some qualitative importance—the application of II and III and their variants appears to explain some interesting general trends in experimental data which are not easy to interpret otherwise.

In this discussion we have limited ourselves to consideration of a three-centre system A + BC. The centres need not of course be atoms, but merely molecular parts which retain their identity during reaction. In more complicated reactions it is frequently found that only three reactive centres are involved in the rate-determining step. When more than three centres are actually involved, treatment along these lines still aids in clarifying the situation, as we shall see, for example, in the hydrolysis of esters.

This necessitates a certain degree of schematisation, which we think is justified by its results, but which should be explicitly stated. For example, if water is an attacking agent and gives a hydroxyl to a positive carbon atom, we regard the water molecule as characterised by a smaller value of the negative $e_A$ than an attacking hydroxyl ion, and we try to see what can be accounted for on this basis. Similarly we regard a weak tertiary base as having a smaller negative $e_A$ than a strong base. We might, on the other hand, regard the system *base plus alkyl halide* as a four-centre system, and consider the development of negative charge on the nitrogen atom as a function of the activation of the base, the electron-pair which has to be loosened from the rest of the molecule itself constituting the fourth centre. This, as Dr. Sutton has pointed out to us, might be a very fruitful mode of approach, especially in those reactions which appear to be determined by the condition that electromeric effects render unshared electrons easily available on a given atom only at the call of the reagent. This problem is referred to later in connexion with the substitution of chlorobenzene, which we are hoping to investigate further.

In the meantime we may test the possibilities of the simple scheme.

*Survey of Experimental Results.*—The above considerations were developed primarily with the object of interpreting two sets of experimental results recently obtained in this laboratory (see following papers). One set refers to the formation of quaternary ammonium salts, the other to the hydrolysis of esters; other examples, however, are also discussed in this section.

As an example of Rule I may be taken the formation of quaternary ammonium salts. Here a pronounced rise in activation energy is found on passing from methyl iodide through ethyl to *iso*propyl iodide: it is attributable to the diminished positive charge on the carbon atom which attracts the approaching base. When we pass from a weak base like pyridine to a strong base like triethylamine, the activation energy falls.* We schematise the difference between the two bases by saying that the stronger base with its more readily available pair of electrons has a greater effective negative charge, *i.e.*, a greater value of $e_A$. (The measured dipole moments are of no help in characterising the bases from this point of view. At large distances, $x$, of a charge from a dipole of moment $\mu = ed$, the force is proportional to $\mu/x^3$, but when $x$ is small compared with $d$, the force tends to become proportional to $e/x^2$. For the close approach involved in chemical interaction the latter is probably nearer the truth.) Rule II allows us to interpret the changes in activation energy found when for a given iodide we go from one base to another, or for a given base from one iodide to another. Table I shows the changes of activation energy (for two solvents) accompanying these variations. It is seen that for methyl iodide the change in $E$ on going from triethylamine to pyridine is greater than that for *iso*propyl iodide. For methyl iodide the factor $e_B$ is larger than for *iso*propyl iodide, the positive charge on the carbon in the

* Compare the fall in $E$ found on passing to a stronger base in the reaction between substituted dimethylanilines and methyl picrate (Hertel and Dressel, *loc. cit.*).

after having been diminished by the flow of electrons from the methyl groups, so that the change in $e_A$ will make a larger change in the repulsion energy and, since changes in $E$ are here determined largely by changes in this, will bring about a larger change in $E$ itself. Similarly, the results show that on passing from one iodide to the other, the changes are greater for triethylamine than they are for pyridine: this is explained as due to the fact that the higher value of $e_A$ for triethylamine makes changes in $e_B$ have a greater influence on the repulsion term and therefore on $E$. Thus it seems that, not only the direction of the changes, but also their relative magnitudes can be interpreted in the light of the above principles.

TABLE I.

*Formation of Quaternary Ammonium Salts.*

(In each case the number in the first line refers to benzene solution, that in the second line to nitrobenzene.)

| | MeI. | $Pr^{\beta}I$. | | $NEt_3$. | $C_5H_5N$. |
|---|---|---|---|---|---|
| $E_{C_5H_5N} - E_{NEt_3}$ | 4600 | 900 | $E_{Pr^{\beta}I} - E_{MeI}$ | 7400 | 3700 |
| | 3900 | 700 | | 6300 | 3100 |

Among other reactions determined mainly by repulsion energy and only to a small extent by bond strength changes may be mentioned the benzoylation of amines, and the acid and alkaline hydrolysis of benzoic esters.

The bond-energy factor also seems less important than the repulsion energy in catalysed prototropic changes: Evans, Morgan, and Watson (J., 1935, 1167) find that the order of energies for the acid-catalysed prototropic change of substituted acetophenones varies *in the direction governed by the attraction of the catalysing proton to the carbonyl oxygen,* although this is the direction of increasing strength of attachment of the mobile hydrogen atom. Since the catalyst is charged and has a large effective $e_A$, this is what we should expect. In another triad prototropic system catalysed by negative ions (ethoxyl) the effect of substituents is the reverse of that found by Nathan and Watson, and thus still in the sense governed by attraction of the negative ion (Shoppee, J., 1933, 1117). But, as Shoppee points out, this case is unusual, since proton attachment and attraction of reagent change in the same sense. Most benzene substitutions probably follow the same rule, but the activation energies are not properly known for the nitration and sulphonation reactions.

We may now consider some interesting cases in which there is a transition from one type of behaviour to another in a way which can be understood in the light of the rules formulated above.

First, we may compare the alcoholysis of acyl chlorides (Branch and Nixon, *loc. cit.*) with the alcoholysis of triarylmethyl chlorides in ether–alcohol solution (Nixon and Branch, *loc. cit.*).* For the former reaction the trend of values is indicated by the following selection:

| | | | |
|---|---|---|---|
| *p*-Nitrobenzoyl chloride ............ | 11,100 | Benzoyl chloride ..................... | 14,400 |
| *p*-Chlorobenzoyl chloride ............ | 13,850 | *p*-Methoxybenzoyl chloride ...... | 18,650 |

Here the introduction of a nitro-group, for example, diminishes the repulsion of the hydroxyl group in the approaching alcohol, while causing the chlorine to be held more tightly. The fact that the activation energy is lowered shows that the change in the repulsive term is the most important. With the alcoholysis of the triarylmethyl chlorides the trend is in the opposite direction:

| | | | |
|---|---|---|---|
| Diphenyl-*p*-tolylmethyl chloride ...... | 12,450 | *p*-Chlorotriphenylmethyl chloride ... | 13,480 |
| Triphenylmethyl chloride ............ | 13,420 | *p*-Nitrotriphenylmethyl chloride ... | 16,710 |

Here the energy of activation increases as the carbon–chlorine bond strength increases, although the repulsion of the approaching hydroxyl or ethoxyl is decreased. The origin of the difference would appear to lie in the fact that the carbonyl carbon of the acyl chlorides bears, through the influence of the oxygen, a larger positive charge than the central

* A similarly contrasted behaviour is shown by the velocities of addition to pyridine of substituted benzyl bromides and substituted bromoacetophenones respectively (Baker, J., 1933, 1128).

carbon atom of the triphenylmethyl halides. It thus attracts the approaching group more powerfully, and in the transition state we have relatively close approach and relatively smaller bond stretching. The activation energy is therefore sensitive to changes in the repulsive term. In the triphenylmethyl halides there is relatively little attraction of the reagent; consequently, the repulsion is considerable, and the compromise reached in the transition state involves a greater proportion of energy as bond energy. Hence the variations in the latter govern the trend of the activation energies.

Interesting transitions are shown by the reactions of the alkyl halides with the following series of reagents: strong tertiary base, weak tertiary base, negative hydroxyl or alkoxyl ion, and water and alcohol molecules. As we have seen, the change from weak base to strong base can be represented as an increase in the effective value of $e_A$ and results in greater dependence on the repulsion term. When we change the reagent attacking an alkyl halide from a tertiary base to a hydroxyl ion, the strength of the carbon–halogen bond is a constant, but the non-electrostatic part of the repulsion energy will change in a difficultly predictable way. We find, in fact, that the activation energy increases very markedly (*e.g.*, pyridine and ethyl iodide 15,800; triethylamine and ethyl iodide 11,400; ethyl iodide and sodium hydroxide 21,000). The increase may be due partly to an increased permanent repulsion of the reagent, but is probably also connected with changes in the repulsion between the products. In the quaternary ammonium salt formation the products are ions, whereas in the hydrolysis they are an ion and a neutral molecule:

$$NEt_3 + CH_3I = [NEt_3CH_3]^+ + I^-$$
$$OH^- + CH_3I = CH_3{\cdot}OH + I^-$$

The total repulsion between the products may therefore be expected to be greater in the latter case, and this raises the activation energy by lifting curve II in Fig. 3 and so increasing the distance $r_1$. Without deciding which factor is more important, we can say that, since the activation energy is much greater, and since the bond to be stretched is the same, then the increase must be due to a change in the repulsive terms. Hence, in accordance with rule III, we should expect the bond energy to play a more important part. In view of the large increase in $E$ this effect should be considerable. But at the same time we have changed from a base to a negative ion: this means a large increase in the effective charge of the reagent, $e_A$. In fact, the experimental results show that the bond strength and repulsion terms become of nearly equal importance, the activation energies of alkyl halides for reaction with hydroxyl ions or alkoxyl ions varying little as one changes from methyl to *iso*propyl (Grant and Hinshelwood, J., 1933, 258; Hughes, Ingold, and Shapiro, J., 1936, 225; Cooper and Hughes, J., 1937, 1183). Some values are: ethyl chloride 23,000 (in alcohol); *iso*propyl chloride 23,000 (in 80% aqueous alcohol); ethyl bromide 21,000 (alcohol); *iso*propyl bromide 20,760 (in 60% alcohol), 21,700 (80% alcohol), the changes of solvent being probably of minor importance in these examples.

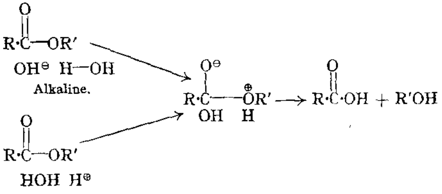
These results are confirmed by those found for the reactions with sodium alkoxides in alcoholic solution, the mechanism being an attack of the $OR^-$ ion on the halide (Segaller, J., 1913, **103**, **1421**; **1914**, **105**, 106; Haywood, J., 1922, **121**, **1904**; Woolf, J., 1937, 1172). The following examples show the approximate constancy of $E$:

| Iodide. | RI + PhONa. | RI + Ph·CH$_2$·ONa. |
|---|---|---|
| Methyl | 22,120 | 20,570 |
| Ethyl | 22,000 | 21,860 |
| *iso*Propyl | 22,100 | 21,410 |

Since the two opposing effects nearly balance when the alkyl halide is attacked by hydroxyl, we should expect the bond-strength factor to be of predominant importance when we pass from hydroxyl to the water molecule as the attacking agent, the value of $e_A$ being here much less. In fact, it is found that the attack by water on *iso*propyl and *tert.*-butyl halides is much easier than with methyl and ethyl halides, the change being in the sense of the change in bond strength. The accumulation of negative charge from the substituent alkyl groups loosens the halogen and should lower the activation energy. Hughes regards this as a change to a unimolecular mechanism in which the reaction is

determined solely by the rate of ionisation of the halide, but on general grounds and in the light of fresh evidence which has appeared since Hughes's paper (Taylor, J., 1937, 1853), we should prefer to regard the change as one depending upon the lowered effective charge of the attacking water molecule. Unfortunately, we can only judge from the course of *velocities* in this case since with the *tert.*-butyl compounds the activation energies for the reaction with $OH^-$ cannot be measured, and with the *iso*propyl compounds the proportion of hydrolysis by water under normal conditions is too small to allow $E$ to be determined with much accuracy. The relative changes in velocity are, however, so marked that they may be taken provisionally as significant. (The large changes of $PZ$ in passing from hydrolysis by alkali to hydrolysis by water are only to be expected, since one of the reactants becomes the solvent in the latter case.) Further, as already mentioned, in the alcoholysis of substituted triarylmethyl chlorides, which are in fact substituted alkyl chlorides, the trend of $E$ is again governed by the bond strength.

In the hydrolysis of esters, the Lowry mechanism, which is generally accepted, makes the following postulates. In alkaline hydrolysis the hydroxyl ion becomes attached to the carbonyl carbon, whereas in acid hydrolysis the proton combines with the ethereal oxygen. The second step in either case involves the obtaining of a second ion from water to supplement the one previously derived from the acid or the alkali. The last step involves the breaking of the bond as shown :




The fact that the mean values of $P$ are the same for both types supports the view that both mechanisms have a similar plan. The effect of substituents is in the same direction in each case, which shows that the charge on the carbonyl carbon matters in the same way in each. But in alkaline hydrolysis the charged ion attacks the carbon atom where the effect of the substituents is greatest, while the water attacks the oxygen where the effect of the substituents is damped down, whereas in acid hydrolysis it is the uncharged water which attacks the carbonyl, and the ion which attacks a point more remote from the substituent. Since the activation energies for acid and alkaline hydrolysis are different, although the bonds formed are identical, it is assumed that the repulsion terms govern the situation and that the attraction or repulsion of an ion is considerably greater than the attraction or repulsion of a water molecule, and further that the influence of the substituent decreases with its distance from the reaction centre.

The following table shows the change in activation emergy to be expected from an electron sink such as a nitro-group in the group R. One minus sign indicates a small lowering and two indicate a great lowering.

| Change in activation energy to be expected on basis of approach of | Alkaline hydrolysis. | Acid hydrolysis. |
|---|---|---|
| (1) Hydroxyl to carbonyl | — — | nil |
| (2) OH of water to carbonyl | nil | — |
| (3) Hydrion to oxygen | nil | + |
| (4) H of water to oxygen | + | nil |

On balance, the alkaline hydrolysis benefits most, which is consistent with the fact that the effect of the substituents is very much greater in alkaline than in acid hydrolysis. It is not surprising that (2) outweighs (3) enough to give a trend of the activation energies

in acid hydrolysis in the same direction as in alkaline hydrolysis (see Part III, Fig. 1). Similar considerations explain why the average activation energies for alkaline hydrolysis are some thousands of calories lower than for acid hydrolysis.

That the facts relating to ester hydrolysis are thus consistent with the view that the repulsive energy is the governing factor, even when water is the agent which attacks the most important centre of charge, is in contrast with what has been said about the alkyl halide hydrolysis. The explanation, as in the transition from triarylmethyl to acyl chlorides, would appear to depend upon the fact that the carbonyl carbon is the seat of a much more important charge than the carbon of an alkyl halide: thus, close approach of a suitable reagent is encouraged, and the balance of the activation energy is shifted away from the bond-stretching term to the repulsive term, and changes in the latter become most significant.

With regard to the problem of benzene substitution, it is a pity that more data about energies of activation are not available. There is, however, little doubt that the attraction of the reagent is in most cases the predominant factor, and this would almost certainly be reflected in the measured activation energies. One point is, however, worth considering further. As is well known, the case of chlorobenzene is anomalous, *op*-substitution being found associated with a decreased reactivity compared with benzene. One explanation is that at the approach of the reagent an electromeric effect occurs, owing to easy polarisability, which renders electrons more easily available than would have been expected from the dipole moment. If this explanation is correct, one would expect a reaction depending upon a time-variable polarisation to be associated with an abnormal value of $P$. If the value of $E$ proved to be abnormally large, it might suggest an alternative explanation, *viz.*, that with chlorobenzene substitution is governed by the loosening of the proton rather than by the approach of the reagent (in accordance with rule III above). Increased repulsion of the reagent would make the reaction slow, but the loosening of the proton would occur most readily at the *o*- and *p*-positions. This mechanism had been assumed by Hückel (*Z. physikal. Chem.*, 1937, *B*, **35**, 163) for benzene substitution generally, where it is not applicable, as Robinson has pointed out: but, in the light of what we have said, it may be admissible as the explanation of an apparent anomaly. All that can be said at the moment is that it would be interesting to investigate further the question of the activation energies involved in the further substitution of chlorobenzene and to compare the kinetics of this reaction carefully with that involved in the substitution of nitrobenzene.

Oxford University. [*Received, March 25th*, 1938.]

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## 167. *The Activation Energy of Organic Reactions. Part II. The Formation of Quaternary Ammonium Salts.*

By K. J. Laidler and C. N. Hinshelwood.

The activation energies have been determined for the reactions of each of two amines with two alkyl iodides. The results are closely parallel for two solvents of different polarity, benzene and nitrobenzene. They are explained in terms of the theory discussed in Part I, changes in the importance of the repulsive energy term being postulated. The variations of log $PZ$, and the solvent influence on the parameters of the Arrhenius equation are also considered.

In the usual Arrhenius equation ($k = PZe^{-E/RT}$), the factor $P$ varies over a very wide range, but it has now been shown that for reactions belonging to one series its variation is not considerable when compared with that of $E$, and when it occurs it can often be explained as due either to a functional relation with $E$ (Fairclough and Hinshelwood, J., 1937, 538), or, in those cases in which the changes of structure are not very small, to ordinary geometrical effects. The variation of $P$ and $E$ in quaternary salt formation has already been studied by Winkler and Hinshelwood (J., 1935, 1147). The object of the present investigation was to determine, in greater detail than was done in that paper, the change

in $E$ with changes in the amine and the halide, and to see how far these can be explained by correlating the modern analysis of activation energy with the theory of electron displacements in organic compounds (see preceding paper).

For this purpose it was decided to study the reactions of two amines of quite different strengths, *viz.*, triethylamine and pyridine, with two iodides in which the carbon–iodine bond strengths differed considerably, *viz.*, methyl and *iso*propyl iodides. In addition, since it was expected that the influence of any electrostatic forces concerned would vary with the solvent, the four reactions were measured in two solvents of widely differing polarity, *viz.*, benzene and nitrobenzene.

Nitrobenzene was purified by distillation, and, in order that no errors should arise from the use of specimens of different purity, was prepared in large quantities at a time; when different specimens were used, these were tested against one another by measuring a given reaction rate in them at two temperatures. "AnalaR" Benzene was used. The reacting substances were fractionated to correct and constant b. p. in an all-glass apparatus; pyridine was dried for some time over potassium hydroxide.

All activation energies were determined from measurements of velocity constants at four temperatures. From 15° to 80° electrically controlled thermostats, constant to less than 0·1°, were used, from 100° to 150° specially constructed boiling-liquid thermostats, and for 5° a Dewar vessel containing melting benzene. Thermometers were compared with N.P.L. standards. With the exception to be mentioned below, the experimental method was to seal up 2 c.c. of each of the reactants, N/5 before mixing, in small glass tubes, immerse them in the thermostats for known times, correcting when necessary for the time required for heating up, and then to analyse the mixtures by washing them into excess of N/50-acid and back-titrating with baryta. The indicators used were methyl-red for triethylamine, and for pyridine a mixture of equal volumes of aqueous 0·1% methyl-orange and 0·02% methylene-blue (Fawcett and Gibson, J., 1934, 396). Glassware was standardised, and all velocity constants were corrected for change of concentration due to expansion of solvent.

*Results.*—Except with one reaction which showed autocatalysis, and with one which went to an equilibrium, satisfactory constants were obtained by applying the ordinary bimolecular formula. Velocity determinations were also made with the reactants diluted five times; within the limits of experimental error no change in constant was found, except in the reaction between triethylamine and *iso*propyl iodide in nitrobenzene, where an increase with dilution was observed. In all cases end-point determinations were made.

The following reactions presented special features.

*Triethylamine and* iso*propyl iodide in benzene.* Here, pronounced autocatalysis was observed, the bimolecular constant rising considerably as the reaction proceeded, this rise being greater at higher temperatures. This is explained by the fact that the reaction only proceeds conveniently in a temperature range in which the salt produced remains partly dissolved in the benzene, making the solvent more polar. The true constant was obtained by plotting that given by the ordinary formula against the corresponding percentage, and extrapolating to zero percentage.

*Triethylamine and methyl iodide in nitrobenzene.* Owing to the high velocity of this reaction, it was necessary to work at a higher dilution, N/25-solutions of each of the reactants being mixed. At 5° this was done with pipettes, at 15° and 25° by breaking a bulb containing one of the reactants inside a tube containing the other, the whole having been immersed in the thermostat for some time, and at 40°, where this method could not be used owing to the high volatility of the methyl iodide, a special mixer was used. The essential feature of this was that the methyl iodide was prevented from escaping by means of a stopper which could be removed when the reaction was to be started. The ordinary method of stopping the reaction was here too slow, the acid being immiscible with nitrobenzene; the method used was to pour in a solution of hydrochloric acid in aqueous acetone, with 50 c.c. of which the nitrobenzene solutions were completely miscible.

*Pyridine and* iso*propyl iodide in nitrobenzene.* This reaction proceeds to an equilibrium. The equilibrium constants at the four temperatures of the reaction were determined, and from them the velocity constants of the forward reaction were calculated from the integrated form of the expression $dx/dt = k_1(a - x)^2 - k_2x$, which is $k_1 = \frac{1}{2\alpha t}\log_e\left[\frac{x - (\beta + \alpha)}{x - (\beta - \alpha)} \cdot \frac{(\beta - \alpha)}{(\beta + \alpha)}\right]$ where $\alpha = \sqrt{aK + K^2/4}$, $\beta = a + K/2$, and $K = k_2/k_1$. The values so obtained were com-

pared with those obtained by the extrapolation to zero reaction of the ordinary bimolecular constants, satisfactory agreement being found (see Table II).

*Triethylamine and* iso*propyl iodide in nitrobenzene.* With this reaction a pronounced increase in velocity constant was found on dilution, the effect being repeated at several temperatures (Table III). We ascribe it to the high sensitivity of the reactions to the solvent, which may in this case be made more polar by the dissolution of the quaternary salt formed. The bimolecular constants obtained were satisfactory; $E$ was measured for a constant dilution.

All of the other cases were straightforward. The numbers in Table I illustrate the type of constant obtained; $x$ is the percentage change, $a$ the initial concentration of amine and iodide,

TABLE I.

| $NEt_3$ and MeI in Ph·$NO_2$ at 39·3°; $a$ = 0·02. | | | $NEt_3$ and $Pr^{\beta}I$ in Ph·$NO_2$ at 60·1°; $a$ = 0·1. | | | $C_5H_5N$ and MeI in $C_6H_6$ at 99·3°; $a$ = 0·1. | | |
|---|---|---|---|---|---|---|---|---|
| $t$ (secs.). | $x$. | $k \times 10^2$. | $t$ (mins.). | $x$. | $k \times 10^5$. | $t$ (mins.). | $x$. | $k \times 10^3$. |
| 325 | 31·4 | 7·06 | 1,580 | 15·7 | 1·97 | 58 | 26·75 | 1·050 |
| 1124 | 60·1 | 6·75 | 4,490 | 33·8 | 1·91 | 80 | 32·75 | 1·005 |
| 1295 | 64·9 | 7·14 | 7,508 | 45·35 | 1·85 | 88 | 35·3 | 1·035 |
| 1530 | 68·8 | 7·20 | 10,036 | 52·9 | 1·88 | 231 | 58·5 | 1·020 |
| 1975 | 73·7 | 7·19 | 14,298 | 61·7 | 1·89 | 244 | 59·75 | 1·014 |
| 2405 | 76·3 | 6·72 | 17,637 | 66·5 | 1·88 | 315 | 65·68 | 1·013 |
| | | | | | | 340 | 67·7 | 1·028 |

TABLE II.

*Details of the reaction between pyridine and* iso*propyl iodide in nitrobenzene* (a = 0·1).

[$k'$ is the value obtained from the ordinary bimolecular formula, $k$ that obtained by the use of the equilibrium formula given in the text.]

| At 60·0°. | | | | At 121·0°. | | | |
|---|---|---|---|---|---|---|---|
| $t$ (mins.). | $x$. | $k' \times 10^5$. | $k \times 10^5$. | $t$ (mins.). | $x$. | $k' \times 10^3$. | $k \times 10^3$. |
| 2,202 | 24·3 | 2·430 | 2·655 | 50 | 26·0 | 1·168 | 1·216 |
| 3,700 | 34·45 | 2·425 | 2·650 | 62 | 30·0 | 1·152 | 1·208 |
| 5,518 | 43·5 | 2·320 | 2·680 | 101 | 40·6 | 1·129 | 1·213 |
| 8,760 | 53·55 | 2·197 | 2·580 | 175 | 52·3 | 1·043 | 1·210 |
| 12,780 | 61·2 | 2·055 | 2·432 | 215·5 | 56·8 | 1·018 | 1·242 |
| 15,450 | 65·2 | 1·960 | 2·415 | 304 | 63·0 | 0·978 | 1·300 |
| Average value of $k = 2·57 \times 10^{-5}$. | | | | Average value of $k = 1·231 \times 10^{-3}$. | | | |
| Extrapolated value of $k' = 2·59 \times 10^{-5}$. | | | | Extrapolated value of $k' = 1·225 \times 10^{-3}$. | | | |

TABLE III.

*The effect of dilution on the constants—typical results.*

| | | | Constant* at $a$ = | | |
|---|---|---|---|---|---|
| Solvent. | Reaction. | Temp. | 0·1. | 0·04. | 0·02. |
| $C_6H_6$ | $NEt_3$ + MeI | 39·75° | $31·11 \times 10^{-4}$ | — | $30·54 \times 10^{-4}$ |
| $C_6H_6$ | $C_5H_5N$ + MeI | 99·3 | $102·4 \times 10^{-5}$ | — | $102·5 \times 10^{-5}$ |
| Ph·$NO_2$ | $NEt_3$ + $Pr^{\beta}I$ | 79·9 | $7·83 \times 10^{-5}$ | $9·47 \times 10^{-5}$ | — |
| | | 100·2 | $26·34 \times 10^{-5}$ | $30·8 \times 10^{-5}$ | — |
| | | 121·1 | $78·0 \times 10^{-5}$ | $90·0 \times 10^{-5}$ | $110·4 \times 10^{-5}$ |

* The constants are uncorrected for solvent expansion.

TABLE IV.

| $NEt_3$ and MeI. | | $NEt_3$ and $Pr^{\beta}I$. | | $C_5H_5N$ and MeI. | | $C_5H_5N$ and $Pr^{\beta}I$. | |
|---|---|---|---|---|---|---|---|
| Temp. | $k \times 10^4$. | Temp. | $k \times 10^6$. | Temp. | $k \times 10^5$. | Temp. | $k \times 10^6$. |
| *In benzene.* | | | | | | | |
| 4·8° | 4·40 | 99·6° | 1·777 | 39·8° | 3·893 | 99·7° | 10·37 |
| 15·0 | 8·05 | 120·4 | 6·370 | 60·0 | 14·60 | 121·0 | 39·00 |
| 24·9 | 14·20 | 137·5 | 15·27 | 80·1 | 52·40 | 138·0 | 109·2 |
| 39·75 | 31·65 | 152·4 | 27·28 | 99·3 | 112·4 | 149·8 | 196·2 |
| *In nitrobenzene.* | | | | | | | |
| 4·1 | 93·5 | 60·1 | 19·50 | 24·8 | 31·76 | 60·0 | 20·45 |
| 15·0 | 181·0 | 79·9 | 82·05 | 39·9 | 98·20 | 80·1 | 112·8 |
| 24·8 | 309·5 | 100·2 | 280·5 | 60·0 | 349·0 | 100·2 | 428·0 |
| 39·9 | 708·5 | 121·1 | 845·5 | 80·3 | 1182·0 | 112·0 | 1333·0 |

TABLE V.

| Solvent : Benzene. | | | | | Solvent : Nitrobenzene. | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Amine. | Iodide. | log ($k_{100°}$ × $10^6$). | $E$. | log $PZ$. | Amine. | Iodide. | log ($k_{100°}$ × $10^6$). | $E$. | log $PZ$. |
| $NEt_3$ | MeI | 4·59 | 9,700 | 4·29 | $NEt_3$ | MeI | 5·94 | 9,700 | 5·65 |
| ,, | $Pr^{\beta}I$ | 0·248 | 17,100 | 4·29 | ,, | $Pr^{\beta}I$ | 2·44 | 16,000 | 5·86 |
| $C_5H_5N$ | MeI | 3·17 | 14,300 | 5·59 | $C_5H_5N$ | MeI | 4·50 | 13,600 | 6·50 |
| ,, | $Pr^{\beta}I$ | 1·03 | 18,000 | 5·62 | ,, | $Pr^{\beta}I$ | 2·62 | 16,700 | 6·43 |

TABLE VI.

*Activation energy differences.*

| | $C_5H_5N-NEt_3$. | | $Pr^{\beta}I$–MeI. | |
|---|---|---|---|---|
| | MeI. | $Pr^{\beta}I$. | $NEt_3$. | $C_5H_5N$. |
| $C_6H_6$ ........... | 4600 | 900 | 7400 | 3700 |
| $Ph\cdot NO_2$ ........ | 3900 | 700 | 6300 | 3100 |

| | $C_6H_6-Ph\cdot NO_2$. | |
|---|---|---|
| | MeI. | $Pr^{\beta}I$. |
| $NEt_3$ ........... | 0 | 1100 |
| $C_5H_5N$ ........ | 700 | 1300 |

and $k$ the bimolecular constant in (l. g.-mol.$^{-1}$ secs.$^{-1}$), uncorrected for solvent expansion. Table IV gives the velocity constants obtained at the various temperatures, corrected for solvent expansion; in each case the Arrhenius equation is satisfactorily obeyed. The final values of $E$, $\log_{10} PZ$, and $\log_{10} (k_{100°} \times 10^6)$ are given in Table V; $E$ is always calculated both from the slope of the line obtained by plotting $\log_{10}k$ against $1/T$, and by the method of least squares, agreement being found in each case.

## DISCUSSION OF RESULTS.

It is seen from the figures in Table V that the most important factor determining the changes in velocity is the energy of activation; for instance, whereas $\log_{10}k_{100°}$ varies by about 5·7, the maximum variation of log $PZ$ is only about 2·2. For small changes in velocity, however, a change in $PZ$ may be of importance; *e.g.*, with *iso*propyl iodide, on changing the base, the change of $PZ$ is seen, in both solvents, to outweigh the change of $E$.

The changes in the energy of activation will be considered first. It is seen from Table VI, which shows the differences between the activation energies for the various changes, that (1) the changes in $E$ on changing the base and on changing the iodide are of the same order in the two solvents; (2) a rise in $E$ is found on passing from triethylamine to pyridine and also (3) on passing from methyl iodide to *iso*propyl iodide; (4) the change of base causes a smaller change in the energy of activation in the reactions with *iso*propyl iodide than in those with methyl iodide; and similarly, (5) the change in $E$ on varying the iodide is less in the reactions with pyridine than in those with triethylamine.

Points (2)—(5) are shown in both solvents, the results illustrating (2) and (3) four times, and (4) and (5) twice each.

(6) With regard to change of solvent, on passing from benzene to nitrobenzene, $E$ falls, except in the case of the triethylamine–methyl iodide reaction, where it remains constant. Moreover, the changes in $E$ on changing one of the reactants are somewhat smaller in nitrobenzene than they are in benzene.

In view of the widely differing polarities of the solvents, (1) is of some significance, since it shows that the results are not seriously distorted by slight deviations from the Arrhenius equation due to the variation of the dielectric constant with the temperature. In addition, since the products of the reactions were in all cases soluble in nitrobenzene but very sparingly soluble in benzene, we may conclude that rate of crystallisation does not affect the observed rate of the change.

Facts (2)—(5) can be explained in terms of the theory explained in the preceding paper. Phenomena (2) and (3) are due to the decreases in $e_A$ and $e_B$ respectively. The former is due to the inductive effect of the methyl groups added to the central carbon atom. The lower $e_A$ for pyridine is connected with its weaker basicity. Facts (4) and (5) are due to a displacement of the relative importance of bond energy and repulsive energy in $E$, an increase in the importance of bond energy being associated with an increase of $E$ itself.

The influence of the solvent is more difficult to interpret. An increased dielectric constant will diminish repulsion energies, and make changes in them less important; and it will also have some effect in decreasing the bond strength. A more important effect still is that solvents of high dielectric constant will tend to solvate the polar salt, in this way stabilising the product, and, in accordance with the principles explained in the preceding paper, lowering the activation energy. These influences compensate for one another to a considerable extent. Since, further, the dielectric constant in the immediate vicinity of the reacting molecules must, for polar and non-polar solvents alike, be less than the average value for a continuous phase, we are probably justified in expecting the solvents to influence the variations in $E$ to a much smaller extent than would be calculated from the influence of dielectric constant on electrostatic forces alone. The one case in which the full polarity of the solvent might be expected to come into play is in the solvation of the polar product; this would explain why the activation energies in nitrobenzene are on the whole slightly lower than those in benzene.

With regard to the changes in log $PZ$, it is found that there is (1) very little change with change of iodide, (2) an increase on passing from triethylamine to pyridine, and (3) an increase on passing from benzene to nitrobenzene.

(1) requires no comment. In (2) the change happens to be in the same direction as the increase in $E$ itself, and might be an example of the correlation of $P$ and $E$ frequently found, although in this case it is perhaps more likely to be a geometrical effect (cf. Winkler and Hinshelwood, *loc. cit.*). (3) is an example of the general influence of polar solvents in increasing $PZ$ in reactions of this type (Fairclough and Hinshelwood, J., 1937, 1573; this vol., p. 236).

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# 168. *The Activation Energy of Organic Reactions. Part III. The Kinetics of Acid Hydrolysis of Esters.*

By E. W. Timm and C. N. Hinshelwood.

The parameters of the Arrhenius equation have been determined for the acid hydrolysis of a series of esters in alcohol–water and acetone–water solvents, and these values are compared with those for the alkaline hydrolysis. Both reactions are facilitated by recession of electrons from the seat of reaction. $E$ is higher in acid hydrolysis and the effect of substituents is smaller; also, $PZ$ increases with $E$ in contrast with the constant value in alkaline hydrolysis. The effect of solvent is apparently opposite in the two cases.

The alkaline hydrolysis of substituted benzoic esters in 85% aqueous alcohol has been studied by Ingold and Nathan (J., 1936, 222) and by Evans, Gordon, and Watson (J., 1937, 1430). Data for four of the corresponding esters, hydrolysed by alkali in 56% aqueous acetone, are given by Newling and Hinshelwood (J., 1936, 1357). These investigations showed that in alkaline hydrolysis the reaction is facilitated by recession of electrons from the seat of reaction, and hence, in the terminology of Ingold, is a Class B reaction. Furthermore, in the *m*- and *p*-substituted series of ethyl benzoates, the $PZ$ factor in the Arrhenius equation (when written $k = PZe^{-E/RT}$) is constant, changes in reaction velocity being entirely due to changes in $E$. Newling and Hinshelwood (*loc. cit.*) concluded that the mean value of $PZ$ was very nearly the same for acid as for alkaline hydrolysis, but from the data then available, chiefly on aliphatic esters, it was impossible to say whether the reaction belonged to Class A or to Class B. The proximity of the substituent and reacting group in these aliphatic esters complicated the picture because of steric effects. It therefore seemed desirable to study the acid hydrolysis of substituted benzoic esters, with a view to determining the effect of substituents on the trend of activation energies, and also whether altered reactivity is due to changes in $E$ alone or to changes in both in $E$ and $PZ$. The chloroacetic esters were also studied,

since a wider range of $E$ was expected in view of the wider range in the dissociation constants of the corresponding acids.

The reactions included in this investigation are the acid hydrolysis of ethyl acetate and the three chloroacetates in ethyl alcohol–water, of nine ethyl benzoates in ethyl alcohol–water and acetone–water, and of three methyl benzoates in methyl alcohol–water.

The ordinary titration methods were used to measure the rates of hydrolysis. In general, 5 c.c. of N/10-ester and 5 c.c. of N/10-catalyst were mixed in approximately 11 c.c. reaction bulbs which were then sealed off and placed in the thermostats. After reaction had proceeded for the desired length of time, the tubes were rapidly cooled and the contents titrated with N/50-baryta or ammonia (in the case of the chloroacetates), bromocresol-purple being used as indicator. In the presence of the phenolic *p*-hydroxy-group this indicator does not give a sharp end-point. By using B.D.H. universal indicator the two-stage titration curve was obtained, from which the titre measuring the quantity of carboxylic acid could be determined.

At these concentrations benzoic esters do not hydrolyse at measurable speed below 60°. To obtain a wide enough temperature range for accurate determinations of $E$ it was necessary to work at temperatures up to 155°. Ordinary soda-glass is very appreciably affected at these temperatures when in contact with aqueous solutions; therefore it was necessary to use Pyrex glass for the reaction tubes.

It was desired to study the hydrolysis in both acetone–water and alcohol–water. Since hydrogen chloride esterifies ethyl or methyl alcohol rapidly at these temperatures it is unsuitable as a catalyst, for in any case it esterifies the alcohol formed as a product of the reaction, and when alcohol is also present as solvent the rapid removal of the catalyst cannot be coped with. To solve these difficulties, benzenesulphonic acid was used, since it possesses the desirable properties both of being practically completely dissociated at these concentrations and of not esterifying alcohols under the conditions used.

The solvents were prepared by diluting 400 c.c. of water to 1 l. with acetone, ethyl alcohol, or methyl alcohol respectively. Distilled water was freed from dissolved carbon dioxide by boiling. Commercial acetone was purified by drying for several days over potassium carbonate and then by fractionation through a 5′ column. Absolute ethyl alcohol was used, the 0·2% of water present being allowed for in making up the solvent. The methyl alcohol was purified by the method of Hartley and Raikes (J., 1925, **127**, 524) using aluminium amalgam.

According to the physical properties, purification of the esters used was carried out in an all-glass still at atmospheric pressure, by reduced pressure distillation, by recrystallisation from ligroin or absolute alcohol, or in the case of ethyl anisate by recrystallisation from the melt. All esters existing in the liquid state at room temperature were first dried over calcium chloride. The purity was checked by complete alkaline hydrolysis, except with the chloroacetates and ethyl *p*-hydroxybenzoate. The purity of the latter was checked by titration of the phenolic group. Table I gives the determined physical properties of the esters, together with those recorded in Beilstein.

At and below 80°, electrically-controlled thermostats were used. At higher temperatures special boilers containing water, perchloroethylene, xylene, or anisole were used. Temperatures were standardised with N.P.L. thermometers. Glassware was standardised. Velocity constants were measured at four or five temperatures, over a range of 55—80°, and were corrected for change of concentration due to thermal expansion of the solvent. The Arrhenius equation was obeyed within the limits of experimental error.

Since the hydrolysis is a reversible reaction, treatment of the results depended upon whether or not it was possible to determine the equilibrium concentration accurately. In the hydrolysis of ethyl acetate in alcohol–water the equilibrium concentration was determined over a 60° temperature range and found to be independent of temperature (zero heat of reaction). It was then possible to use the integrated form of the equation

$$dx/dt = k_1[H^+](a - x) - k_2[H^+]x \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

namely,

$$k_1 = (2{\cdot}303\xi/[H^+]at) \log_{10} \xi/(\xi - x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $\xi$ is the amount changed at equilibrium, to determine $k_1$ accurately. The concentration of water and alcohol does not change detectably during the reaction and is therefore not included in the equation. All velocity constants are expressed in l. g.-mol.$^{-1}$ sec.$^{-1}$. It is not possible, in general, to determine the equilibrium concentrations accurately because of the

long time required for equilibrium to be reached, during which time side reactions may become appreciable; it is necessary in these cases to use the equation

$$dx/dt = k[H^+](a - x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

in the integrated form

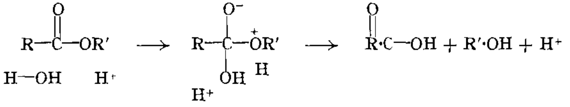
$$k = (2{\cdot}303/[H^+]t) \log_{10} a/(a - x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

In alcohol–water, values of $k$ calculated by (4) will fall as the reaction proceeds. It is then necessary to plot $k$ against percentage of products formed and extrapolate to zero percentage change; $k$ calculated from the initial slope of the percentage change–time curve serves as a check on this method. This fall in $k$ is largely due to esterification of the solvent alcohol molecules by the acid formed from hydrolysis. In acetone–water, hydrolysis will proceed much further, since only the products tend to reverse the reaction. Over the first 30% of reaction this fall is inappreciable and values of $k$ can be averaged. Table II shows values of $k_1$ for the hydrolysis of ethyl acetate at 80·10°, calculated by formula (2), and Table III shows $k_1$ and $k$ for each temperature [calculated by formulæ (2) and (4) and corrected for solvent expansion], and the corresponding values of $E$ calculated by the method of least squares. Values of $k$ calculated from the rate equation, $\log_{10}k_1 = 7{\cdot}525 - 16{,}200/\boldsymbol{R}T$, are included for comparison. Table IV gives the constants and the corresponding temperature for the other esters. In Table V the values of $E$, $\log_{10}PZ$ and $\log_{10}(k_{100^\circ} \times 10^6)$ are collected.

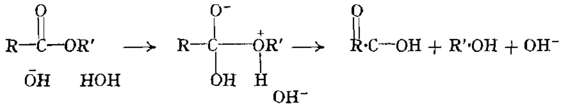
## Discussion.

*The Effect of Substituents on* E.—In acid hydrolysis the activation energy is lowered by substituents which attract electrons (electron sinks) and raised by electron sources; *i.e.*, acid hydrolysis is a Class B reaction. The order of the *p*-substituents in their effect on $E$ is that generally found, *viz.*, $OCH_3$, $CH_3$, (H), Halogen, $NO_2$. The *m*-nitro-group falls between the *p*-nitro-group and the unsubstituted ester, also in agreement with expectations. The fact that acid and alkaline hydrolysis are both Class B reactions is clearly set forth in Fig. 1, where the activation energies for the acid hydrolysis of *p*-substituted esters are plotted as abscissæ and the activation energies for the alkaline hydrolysis of the corresponding esters are plotted as ordinates. This grouping about a line indicates behaviour approximating to the relationship $\Delta E_{acid} = \alpha \Delta E_{alkaline}$ (Hinshelwood, J., 1937, 635). In Part I the smaller effects of substituents and the higher activation energies in acid hydrolysis are explained by considering the relative repulsions on the proton and water molecule in acid hydrolysis, and on the hydroxyl ion and water molecule in alkaline hydrolysis. The Lowry mechanism is as follows:

*Acid hydrolysis.*



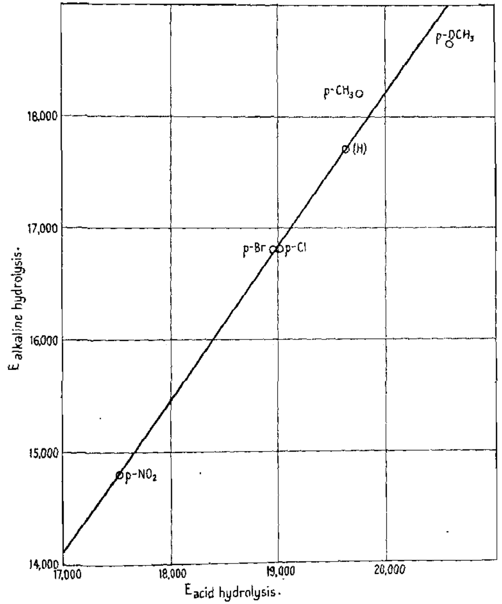
*Alkaline hydrolysis.*



It was shown that in acid hydrolysis the most important step involves the overcoming of the repulsion of an approaching water molecule from which a hydroxyl group must be obtained, whereas in alkaline hydrolysis the corresponding process involves the free hydroxyl ion.

*Relation of* PZ *and* E.—In Fig. 2, $\log_{10}k$ is plotted against $E$ both for the acid and for the alkaline hydrolysis of *m*- and *p*-substituted benzoic esters in alcohol–water. The results for alkaline hydrolysis are those of Ingold and Nathan (*loc. cit.*) and Evans, Morgan, and Watson (*loc. cit.*). As previously stated, in the alkaline hydrolysis changes in $k$ are due to changes in $E$ alone, shown by the fact that the points lie on the line of slope $-2{\cdot}303/RT$ which corresponds to constant $PZ$. In contrast, in the acid hydrolysis the points are grouped about a line considerably steeper than the line of standard slope: this corresponds to an increase of $PZ$ with $E$. Fig. 3 shows how $\log_{10}PZ$ is related to $1/\sqrt{E}$. A functional relation of this type may be explained on statistical grounds (Fairclough and

Fig. 1.

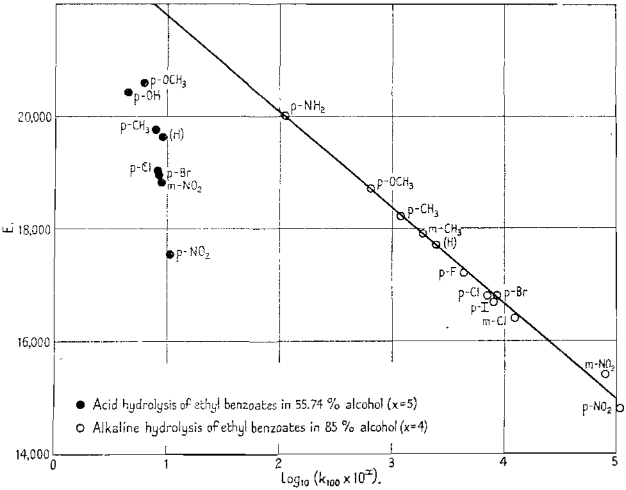



Hinshelwood, J., 1937, 538) by assuming that the average time required for reaction is large compared with the average duration of the collision, this relative time condition varying with the mechanism of reaction so that the increase of $PZ$ with $E$ sometimes does and sometimes does not occur on substitution (see Part I). Considering the wide range over which $PZ$ may vary in general, we may say that here it is substantially the same for acid and for alkaline hydrolysis so long as the solvent remains the same (cf. Newling and Hinshelwood, *loc. cit.*, and present results for acetone–water solvent). This is evidence in favour of the Lowry mechanism, which postulates a similar plan for the two reactions.

The change of $PZ$ with $E$ counteracts the effect of $E$ to a certain extent, but with the benzoic esters, except the *o*-nitrobenzoate, the velocity constants at 100° follow the trend of $E$. The *o*-nitrobenzoate has both a high value of $E$ and a low value of $PZ$. It appears

that here the proximity of the nitro-group reduces $k$ both by decreasing $PZ$ and by raising $E$, although from its electronic nature we would expect $E$ to be lowered. In the chloroacetic esters the $PZ$ factor increases markedly with $E$, so that the effects of changes in $E$ and $PZ$ are practically counterbalanced, as shown in the close grouping of the values for $k_{100°}$. Steric factors apparently work in conjunction with the general factors operating in the *m*- and *p*-substituted benzoic esters in bringing about this large increase of $PZ$ with $E$. This series shows the advantage of comparing activation energies rather than velocity constants at a given temperature. At 100°, $k$ varies only slightly and in a random

FIG. 2.

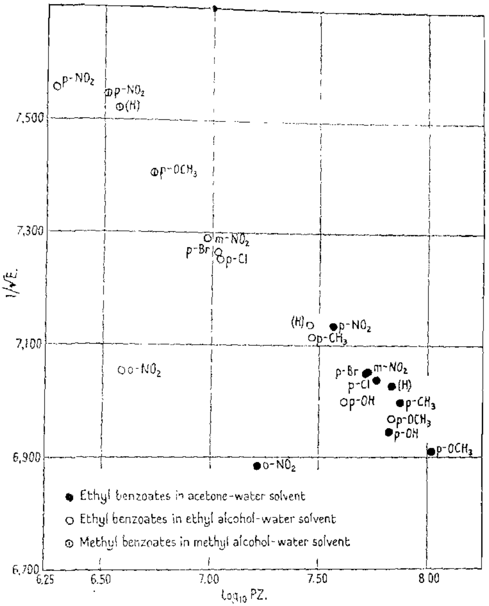



manner, while the activation energy decreases as successive chlorine atoms are introduced into the acetyl group, in accordance with expectations based upon the application of the electronic theory.

TABLE I.

| | Values determined. | | Values given in Beilstein. | |
|---|---|---|---|---|
| | M. p. | B. p. | M. p. | B. p. |
| Ethyl anisate | 6·8° | — | 7·0° | — |
| Ethyl *p*-hydroxybenzoate | 113·5 | — | 112·5—115 | — |
| Ethyl *p*-toluate | — | 111°/13 mm. | — | 235·5°/760 mm. |
| Ethyl benzoate | — | 213 | — | 211—212 |
| Ethyl *p*-chlorobenzoate | — | 122/15 mm. | — | 238 |
| Ethyl *p*-bromobenzoate | (100% hydrolysis only) | | | |
| Ethyl *p*-nitrobenzoate | 56·5 | — | 57 | — |
| Ethyl *m*-nitrobenzoate | 46·7 | — | 47 | — |
| Ethyl *o*-nitrobenzoate | 30·0 | 149/10 mm. | 30 | 149/10 mm. |
| Methyl anisate | 47·7 | — | 47 | — |
| Methyl benzoate | — | 197—198 | — | 198—199 |
| Methyl *p*-nitrobenzoate | 96·2 | — | 96 | — |
| Ethyl acetate | — | 76·9—77·1 | — | 77·1 |
| Ethyl chloroacetate | — | 143·8—144·2 | — | 144 |
| Ethyl dichloroacetate | — | 157·3—158·0 | — | 158 |
| Ethyl trichloroacetate | — | 167·5 | — | 167·8 |

FIG. 3.




*Solvent Effects.*—In acid hydrolysis the activation energy of a given ester increases as we go from alcohol-water to acetone-water solvent, whereas in alkaline hydrolysis this trend is reversed. Another fact also emerges, *viz.*, that the effect of substituents is greater in alcohol-water. These effects must be related to the manner in which the potential field due to the solvent molecules affects the repulsion energies between and the bond energies of the reactants. Until our knowledge of the liquid state is greater, it is difficult to say more by way of explaining these differences.

TABLE II.

*Acid hydrolysis of ethyl acetate.*

Values of $k_1$ from formula (2) at 80·10°; $t$ is the time in seconds, $x$ and $\xi$ the concentrations of products at time $t$ and at equilibrium respectively, and $k_1$ the bimolecular constant. $100 \times \xi/a = 40{\cdot}2$.

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $t$ | 645 | 900 | 1140 | 1440 | 1740 | 2040 | 2280 | 2640 |
| $100x/\xi$ | 20·13 | 28·61 | 33·00 | 41·05 | 47·08 | 52·80 | 58·25 | 61·50 |
| $k_1 \times 10^6$ | 2815 | 3026 | 2840 | 2965 | 2956 | 2975 | 3095 | 2920 |
| $t$ | 3240 | 3840 | 4440 | 5040 | 5670 | 6660 | 7440 | |
| $100x/\xi$ | 69·85 | 75·80 | 80·30 | 83·70 | 87·35 | 90·10 | 93·25 | |
| $k_1 \times 10^6$ | 2990 | 2986 | 2958 | 2906 | 2943 | 2806 | 2927 | |

$k_1 \times 10^6$ (average) = 2941 (uncorrected for expansion).

### TABLE III.

*Temperature coefficient in acid hydrolysis of ethyl acetate.*

| | | | | |
|---|---|---|---|---|
| Temp. | 24·86° | 39·80° | 60·09° | 80·10° |
| $k_1 \times 10^6$ [average from (2)] | 42·6 | 167·9 | 788 | 3119 |
| $k \times 10^6$ [extrapolated from (4)] | 43·3 | 173·7 | 780 | 3158 |
| $k \times 10^6$ (calc., Arrhenius) | 43·8 | 161·4 | 785 | 3163 |

$E$ (from $k_1$) = 16,200; $E$ (from $k$) = 16,130.

### TABLE IV.

*Acid Hydrolysis of Esters.*

(a) *Ethyl esters in ethyl alcohol–water solvent.*

| Temp. | $k \times 10^6$. | Temp. | $k \times 10^6$. | Temp. | $k \times 10^6$. |
|---|---|---|---|---|---|
| Chloroacetate. | | Dichloroacetate. | | Trichloroacetate. | |
| 24·86° | 39·48 | 24·86° | 21·26 | 24·84° | 82·6 |
| 39·79 | 134·8 | 39·79 | 65·9 | 39·97 | 238·6 |
| 60·04 | 619 | 60·04 | 270·4 | 60·34 | 761 |
| 80·10 | 2259 | 80·10 | 925 | 80·15 | 2166 |
| Anisate. | | *p*-Hydroxybenzoate. | | *p*-Toluate. | |
| 60·00 | 2·05 | 80·20 | 9·92 | 60·05 | 3·24 |
| 80·20 | 14·10 | 99·50 | 41·6 | 80·25 | 16·5 |
| 99·40 | 56·5 | 120·0 | 191·0 | 99·90 | 81·9 |
| 119·9 | 257 | 138·5 | 570 | 120·3 | 301 |
| 138·1 | 800 | | | 139·7 | 978 |
| Benzoate. | | *p*-Chlorobenzoate. | | *p*-Bromobenzoate. | |
| 60·00 | 3·92 | 80·30 | 18·65 | 80·20 | 20·0 |
| 80·20 | 20·5 | 100·00 | 81·2 | 100·00 | 86·2 |
| 99·60 | 84·5 | 120·6 | 312 | 120·2 | 302 |
| 120·2 | 335 | 139·3 | 861 | 139·4 | 955 |
| 138·6 | 1140 | | | | |
| *p*-Nitrobenzoate. | | *m*-Nitrobenzoate. | | *o*-Nitrobenzoate. | |
| 80·20 | 28·6 | 80·20 | 20·9 | 80·30 | 1·495 |
| 98·90 | 103·8 | 99·45 | 88·5 | 100·00 | 5·91 |
| 119·3 | 332 | 119·9 | 332 | 120·6 | 26·2 |
| 138·0 | 952 | 138·3 | 900 | 138·9 | 85·6 |

(b) *Ethyl esters in acetone–water solvent.*

| | | | | | |
|---|---|---|---|---|---|
| Anisate. | | *p*-Hydroxybenzoate. | | *p*-Toluate. | |
| 60·00 | 1·98 | 80·20 | 9·82 | 80·30 | 16·79 |
| 80·20 | 13·38 | 99·80 | 46·9 | 100·05 | 83·1 |
| 99·20 | 58·3 | 120·2 | 196 | 120·5 | 349 |
| 119·9 | 256 | 138·9 | 668 | 138·9 | 1051 |
| 138·5 | 875 | | | | |
| Benzoate. | | *p*-Chlorobenzoate. | | *p*-Bromobenzoate. | |
| 30 | 20·9 | 80·30 | 18·49 | 60·05 | 3·40 |
| `0 | 94·4 | 99·85 | 87·5 | 80·20 | 18·5 |
| [illegible] | 396 | 120·2 | 355 | 100·15 | 86·4 |
| [illegible] | 1293 | 139·4 | 1177 | 120·2 | 346 |
| | | | | 139·2 | 1115 |
| …zoate. | | *m*-Nitrobenzoate. | | *o*-Nitrobenzoate. | |
| | 4·38 | 60·00 | 3·48 | 80·30 | 1·46 |
| | 27·1 | 80·20 | 19·3 | 99·85 | 7·04 |
| | 108·6 | 99·90 | 86·4 | 120·7 | 32·2 |
| | 420 | 120·4 | 368 | 139·2 | 107·6 |
| | 382 | 139·0 | 1150 | | |

(c) *Methyl esters in methyl alcohol–water solvent.*

| | | | |
|---|---|---|---|
| Benzoate. | | *p*-Nitrobenzoate. | |
| 100·20 | 168 | 100·12 | 165 |
| 121·20 | 556 | 120·75 | 574 |
| 139·2 | 1564 | 138·4 | 1538 |
| 153·9 | 3207 | 153·0 | 3175 |

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**Ethyl anisate** ..............
**Ethyl *p*-hydroxybenzoate**
**Ethyl *p*-toluate** ..............
**Ethyl benzoate** ...............
**Ethyl *p*-chlorobenzoate** ....
**Ethyl *p*-bromobenzoate** ....
**Ethyl *p*-nitrobenzoate** ........
**Ethyl *m*-nitrobenzoate** ........
**Ethyl *o*-nitrobenzoate** ........
**Methyl anisate** ..................
**Methyl benzoate** ...............
**Methyl *p*-nitrobenzoate** ......
**Ethyl acetate** ........................108·8
**Ethyl chloroacetate** ............392
**Ethyl dichloroacetate** .........)06
**Ethyl trichloroacetate** .........592

TABLE V.

*Acid Hydrolysis.*

| Ester. | $\log_{10} k_{100°} \times 10^6$. | $\log_{10} PZ$. | *E* (cals.). |
|---|---|---|---|
| (a) *In ethyl alcohol–water solvent.* | | | |
| Ethyl acetate | 4·03 | 7·53 | 16,200 |
| Ethyl chloroacetate | 3·86 | 6·86 | 15,350 |
| Ethyl dichloroacetate | 3·44 | 5·82 | 14,300 |
| Ethyl trichloroacetate | 3·74 | 4·94 | 12,280 |
| Ethyl anisate | 1·79 | 7·84 | 20,590 |
| Ethyl *p*-hydroxybenzoate | 1·65 | 7·62 | 20,420 |
| Ethyl *p*-toluate | 1·89 | 7·47 | 19,760 |
| Ethyl benzoate | 1·955 | 7·46 | 19,630 |
| Ethyl *p*-chlorobenzoate | 1·90 | 7·04 | 19,010 |
| Ethyl *p*-bromobenzoate | 1·92 | 7·03 | 18,950 |
| Ethyl *p*-nitrobenzoate | 2·025 | 6·29 | 17,520 |
| Ethyl *m*-nitrobenzoate | 1·945 | 6·98 | 18,820 |
| Ethyl *o*-nitrobenzoate | 0·71 | 6·59 | 20,100 |
| (b) *In acetone–water solvent.* | | | |
| Ethyl anisate | 1·79 | 8·07 | 20,950 |
| Ethyl *p*-hydroxybenzoate | 1·67 | 7·83 | 20,730 |
| Ethyl *p*-toluate | 1·91 | 7·88 | 20,420 |
| Ethyl benzoate | 1·97 | 7·84 | 20,250 |
| Ethyl *p*-chlorobenzoate | 1·95 | 7·77 | 20,190 |
| Ethyl *p*-bromobenzoate | 1·93 | 7·72 | 20,120 |
| Ethyl *p*-nitrobenzoate | 2·06 | 7·57 | 19,650 |
| Ethyl *m*-nitrobenzoate | 1·95 | 7·73 | 20,110 |
| Ethyl *o*-nitrobenzoate | 0·85 | 7·22 | 21,100 |
| (c) *In methyl alcohol–water solvent.* | | | |
| Methyl anisate | 2·038 | 6·73 | 18,240 |
| Methyl benzoate | 2·206 | 6·57 | 17,690 |
| Methyl *p*-nitrobenzoate | 2·220 | 6·52 | 17,570 |

OXFORD UNIVERSITY. [*Received, March 25th,* 1938.]

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## 169. *Studies in the Sterol Group. Part XXXVII. The Structure of Lumisterol and its Stereoisomers.*

By I. M. HEILBRON, T. KENNEDY, F. S. SPRING, and G. SWAIN.

A constitutional study of lumisterol has necessitated the preparation of the epimers of lumisterol, ergosterol, and dehydroergosterol.

Reduction of ergostatrienone (IV) gives a molecular complex of ergosterol and *epi*ergosterol, reduction of the carbonyl group being accompanied by migration of the $\Delta^4$-ethylenic linkage. *epi*Ergosterol is extremely unstable, quickly isomerising to an ergostatrienol, m. p. 152°, which does not contain a system of conjugated ethylenic linkages. The compound was previously prepared by Marker, Kamm, Laucius, and Oakwood and, as shown by Windaus and Buchholz, was erroneously described by the American authors as "*epi*ergosterol." The view of Windaus and Buchholz that the trienol, m. p. 152°, is a *direct* reduction product of ergostatrienone is, however, incorrect.

Oxidation of lumisterol gives the αβ-unsaturated ketone lumistatrienone (IV), reduction of which gives a molecular complex of lumisterol and *epi*lumisterol, the $\Delta^4$-ethenoid linkage migrating to the $\Delta^5$-location during the course of reduction. Resolution of this complex by means of digitonin readily gives the two components; in contrast to *epi*ergosterol, *epi*lumisterol is relatively stable.

Oxidation of dehydroergosterol gives the αβ-unsaturated *ketone ergostatetraenone* (VII). Reduction of the latter yielded a molecular complex of dehydroergosterol and *epi*dehydroergosterol.

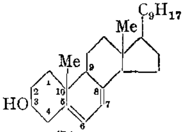
In view of the non-identity (a) of *epi*ergosterol with either lumisterol or pyrocalciferol and (b) of *epi*lumisterol with either ergosterol or *iso*pyrocalciferol, it is concluded that the four stereoisomers, ergosterol, lumisterol, pyrocalciferol, and *iso*pyrocalciferol,

differ solely in the orientation around the two asymmetric centres $C_9$ and $C_{10}$ and not around $C_3$.

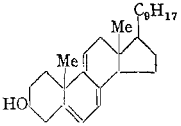
A preliminary study of the enol-acetates of polyunsaturated steroid ketones has been made; the enol-acetates of ergostatrienone, *iso*ergostatrienone, ergostatetraenone and lumistatrienone are described.

LUMISTEROL, a stereoisomer of ergosterol, has been shown to differ from the latter in the orientation of the groups attached to $C_{10}$, and possibly in the orientation around $C_9$. This decision was made by Windaus and Dimroth (*Ber.*, 1937, **70**, 376), who showed that, of the four stereoisomers known whose structure is represented by (I), ergosterol and *iso*pyrocalciferol both give dehydroergosterol (II) (Müller, *Z. physiol. Chem.*, 1935, **231**, 75) on treatment with mercuric acetate, whereas similar treatment of lumisterol and pyrocalciferol gives dehydrolumisterol (Heilbron, Spring, and Stewart, J., 1935, 1221). The conversion of calciferol (III) into the isomeric pyrocalciferols (I) clearly involves the appearance of two new centres of asymmetry within the molecule ($C_9$ and $C_{10}$) and the German authors considered that the four theoretically possible isomers differing in the relative orientation of these two asymmetric centres are represented by ergosterol, lumisterol, pyrocalciferol, and *iso*pyrocalciferol. The orientations of both $C_9$ and $C_{10}$ in the case of ergosterol being indicated by +, the following is an expression of the relationships suggested:

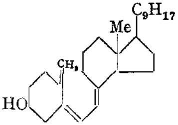
| | $C_9$. | $C_{10}$. | | $C_{10}$. |
|---|---|---|---|---|
| Ergosterol | + | + | → Dehydroergosterol (II) | + |
| *iso*Pyrocalciferol | − | + | | |
| Lumisterol | +(?) | − | → Dehydrolumisterol (II) | − |
| Pyrocalciferol | −(?) | − | | |



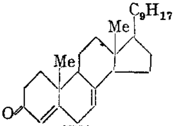
(I.)



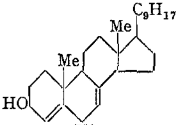
(II.)



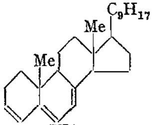
(III.)



(IV.)



(V.)



(VI.)

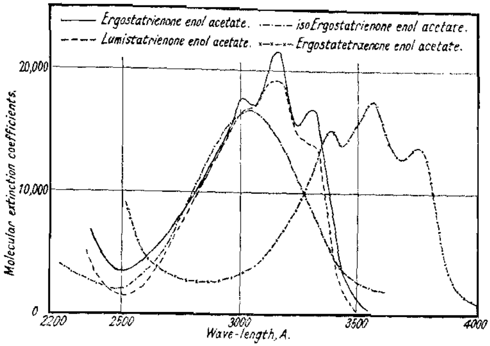
Theoretically, an equally valid interpretation of the reactions of the four isomers under discussion is obtained if it be assumed that they represent the possible stereoisomers obtained by varying the orientation around $C_3$ and $C_9$. According to this view we obtain the following representation:

| | $C_3$. | $C_9$. | | $C_9$. |
|---|---|---|---|---|
| Ergosterol | + | + | → Dehydroergosterol | + |
| *iso*Pyrocalciferol | + | − | | |
| Lumisterol | − | +(?) | → Dehydrolumisterol | − |
| Pyrocalciferol | − | −(?) | | |

If this representation is correct, *epi*ergosterol must be identical with either lumisterol or pyrocalciferol (according to the orientation around $C_9$), and similarly *epi*lumisterol must be identical with either ergosterol or *iso*pyrocalciferol. Furthermore, dehydroergosterol and dehydrolumisterol according to this view are epimers. The preparation of *epi*ergosterol *epi*lumisterol, and *epi*dehydroergosterol has therefore been undertaken in order to effect the necessary comparisons.

The oxidation of ergosterol to an ergostatrienone was first described by Oppenauer (*Rec. Trav. chim.*, 1937, **56**, 137) and later, using a more tedious route, by Wetter and Dimroth (*Ber.*, 1937, **70**, 1665). Ergostatrienone shows the typical light absorption properties of an αβ-unsaturated ketone and is therefore formulated as (IV), migration of the $\Delta^5$-ethenoid linkage of ergosterol (I) having occurred during the oxidation.

FIG. 1.

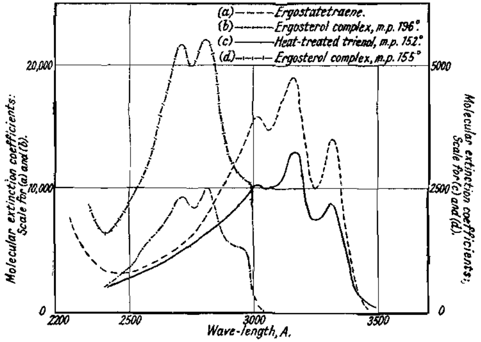



The reduction of ergostatrienone by the Ponndorf–Meerwein method was described by Marker, Kamm, Laucius, and Oakwood (*J. Amer. Chem. Soc.*, 1937, **59**, 1840); they reported that resolution of the crude reduction product by means of digitonin gave ergosterol and an isomeric ergostatrienol, m. p. 152°, which, unlike the former, does not give an insoluble digitonide and consequently was designated "*epi*ergosterol." More recently, Windaus and Buchholz (*Ber.*, 1938, **71**, 576) have shown that the ergostatrienol, m. p. 152°, does not exhibit selective absorption between 2400 and 3000 A., and therefore cannot contain the conjugated system of ethylenic linkages present in ergosterol. They therefore conclude that the reduction of ergostatrienone occurs without migration of an ethylenic linkage, that the trienol, m. p. 152°, has the structure (V), and that the ergosterol isolated by Marker *et al.* is not a true reaction product but is present as a contaminant in the ergostatrienone employed.

Before the appearance of the paper of Windaus and Buchholz, we had completed a detailed study of the reduction of ergostatrienone, using the method employed by Marker *et al.*, and whilst we agree with the former authors that the ergostatrienol, m. p. 152°, of Marker is not *epi*ergosterol, our results show that certain of the views of the German authors require modification. Reduction of ergostatrienone, m. p. 132°, $[\alpha]_D^{20°}$ − 0·8°, with aluminium *iso*propoxide gives a molecular complex which after three crystallisations has the constant melting point 196°. This complex is spectroscopically identical (Fig. 2) with ergosterol, but on standing its melting point rapidly decreases to a minimum value of approximately 155° and this change is accompanied by a marked decrease in the intensity of the light absorption, which finally reaches a value approximately half that of ergosterol. Resolution of either the complex, m. p. 196°, or that of m. p. 155° by means of digitonin gives in each case an insoluble digitonide in approximately 50% yield, which on decomposition by the pyridine method readily gives ergosterol. Thus there can be no possible doubt that ergosterol is obtained as one of the products of reduction of ergostatrienone. The digitonin non-precipitable fraction from each complex readily gave the ergostatrienol, m. p. 152°, described by Marker *et al.*; this compound is spectroscopically transparent and therefore cannot contain a conjugated system of ethenoid linkages.

A consideration of the foregoing facts establishes that reduction of ergostatrienone gives in the first place a mixture of ergosterol and *epi*ergosterol, or, in other words, the reduction of the carbonyl group is accompanied by a facile and complete migration of the $C_4$–$C_5$ linkage to the $C_5$–$C_6$ position. Furthermore, *epi*ergosterol is very unstable, readily isomerising to the trienol, m. p. 152°. It is not possible to decide between the several possible structures for this compound from the available evidence.

FIG. 2.

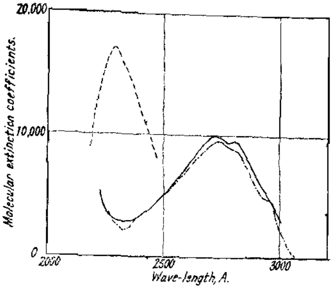



Although it has not been possible to isolate *epi*ergosterol other than in the form of its complex with ergosterol, its instability shows that it cannot be identical with either lumisterol or pyrocalciferol. The latter has been shown to isomerise on irradiation with ultra-violet light to photopyrocalciferol, which resembles the trienol, m. p. 152°, in its spectroscopic transparency (Dimroth, *Ber.*, 1937, **70**, 1621). Thus the change pyrocalciferol ⟶ photopyrocalciferol resembles that of *epi*ergosterol ⟶ trienol, m. p. 152°, in that a migration of one or both of the $C_5$–$C_6$ and $C_7$–$C_8$ ethylenic linkages has occurred with the production of a non-conjugated system. As photopyrocalciferol is reconverted into pyrocalciferol by heat treatment, it appeared possible that similar treatment of the trienol, m. p. 152°, would yield *epi*ergosterol. We find, however, that the trienol, m. p. 152°, gives a product which exhibits absorption in the ultra-violet with a maximum at 3165 A. (Fig. 2). Prolonged treatment of the trienol, m. p. 152°, with acetic anhydride gives an *ergostatetraene*, m. p. 104°, differing from the isomeric hydrocarbons described by Rygh (*Z. physiol. Chem.*, 1929, **185**, 99) and Stoll (*ibid.*, 1931, **202**, 233) and showing the same characteristic absorption as the product from the trienol, but in approximately ten-fold intensity (Fig. 2). In view of the similarity in the absorption spectrum of this ergostatetraene with that of both dehydroergosterol and the enol-acetate of the ergostatrienone described below, we conclude that it has the structure (VI).

Oxidation of lumisterol with aluminium *tert.*-butoxide in the presence of acetone gives *lumistatrienone*, m. p. 139—140°, characterised by its *semicarbazone*, m. p. 247°. Lumistatrienone shows the typical light absorption properties of an αβ-unsaturated ketone (Fig. 3) and is therefore a stereoisomer of ergostatrienone (IV). Reduction of lumistatrienone by the Ponndorf–Meerwein method gives a molecular complex, m. p. 159·5°, which is spectroscopically identical with lumisterol. Resolution of the complex by means of digitonin gives an insoluble digitonide which on decomposition with pyridine yields *epilumisterol*, m. p. 109—110° (*acetate*, m. p. 114—115°), showing the same absorption spectrum as lumisterol. Although the melting points of *epi*lumisterol and its acetate are very close to those of *iso*pyrocalciferol (112—115°) and its acetate (113—115°), the optical rot-

ations differ greatly. Furthermore, a strong depression in melting point was observed on mixing the acetates of *epi*lumisterol and *iso*pyrocalciferol. After removal of the digitonide of *epi*lumisterol the mother-liquors readily gave lumisterol. Thus once again it is established that reduction of the carbonyl group of a steroid ketone of type (IV) is accompanied by migration of the $\Delta^4$-ethenoid linkage into the conjugated $\Delta^5$-location.

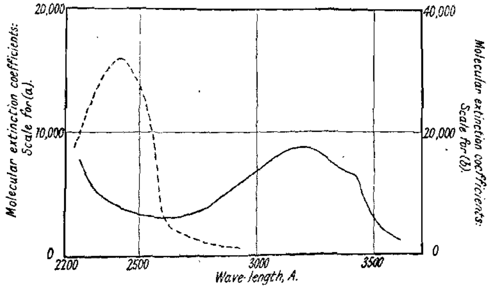
Fig. 3.




- - - - Lumistatrienone.
——·—— epiLumisterol.
———— Lumisterol–epilumisterol complex.

Oxidation of dehydroergosterol by the Oppenauer method gives *ergostatetraenone* (VII), m. p. 140—142°, which also exhibits the characteristic absorption spectrum of an αβ-unsaturated ketone (Fig. 4). Reduction of this ketone with aluminium *iso*propoxide gives a molecular complex of dehydroergosterol and *epi*dehydroergosterol which, when freshly prepared, exhibits an absorption spectrum similar to that of dehydroergosterol

Fig. 4.



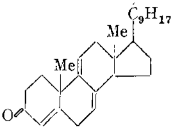

(a)———— Dehydroergosterol–epidehydroergosterol complex.
(b)- - - - Ergostatetraenone.

(Fig. 4). Resolution by means of digitonin readily gives dehydroergosterol, but *epi*-dehydroergosterol, like *epi*ergosterol, is apparently unstable, since the product obtained from the non-digitonide forming fraction of the reduction product exhibits a light absorption of approximately one-fifth of that of dehydroergosterol. The amount of material at our disposal was too small to permit of a complete examination of this

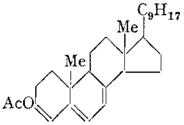
product. It is clear, however, that reduction of the carbonyl group of ergostatetraenone is again accompanied by a migration of the $\Delta^4$-ethenoid linkage to the $\Delta^5$-location.

Since *epi*ergosterol is not identical with either lumisterol or pyrocalciferol, and *epi*lumisterol is not identical with either ergosterol or *iso*pyrocalciferol, the structures assumed by Windaus and Dimroth (*loc. cit.*) for lumisterol, ergosterol, and the pyrocalciferols are substantiated, the stereovariants being $C_9$ and $C_{10}$ and not $C_3$.

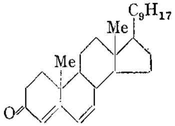
*Enol-Acetates of Steroid Ketones.*—Acetylation of ergostatrienone yields an *enol-acetate*, m. p. 146°, which exhibits an intense light absorption maximum at 3165 A. (Fig. 1) and to which is consequently allocated the structure (VIII). Hydrolysis of this enol-acetate gives *iso*ergostatrienone (IX), previously prepared by Wetter and Dimroth (*loc. cit.*) by the action of methyl-alcoholic hydrogen chloride on ergostatrienone. *iso*Ergostatrienone gives an *enol-acetate*, m. p. 137°, which exhibits an absorption maximum at 3040 A. (Fig. 1), and to which we ascribe the structure (X). We have also examined the acetylation of lumistatrienone, from which an *enol-acetate* has been obtained, m. p. 98°, spectroscopically identical with the enol-acetate of ergostatrienone, and which may therefore be represented by the structure (VIII). The *enol-acetate* of ergostatetraenone, m. p. 161° exhibits an absorption maximum at 3560 A. (Fig. 1), in consequence of which we favour the structure (XI) for this compound.




(VII.)

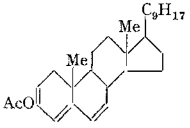


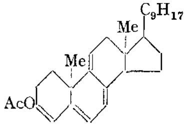

(VIII.)




(IX.)

(X.)




(XI.)

## Experimental.

*Reduction of Ergostatrienone.*—The ketone prepared by the method of Oppenauer, after three crystallisations from light petroleum (b. p. 40—60°)–acetone (5 : 1), had m. p. 132°, $[\alpha]_D^{20°}$ − 0·8° ($l$ = 1, $c$ = 3·2 in chloroform). *Light absorption in alcohol:* maxima, (a) 2300 A., log ε = 4·30; (b) 3200 A., log ε = 1·61. The ketone (10 g.) in *iso*propyl alcohol (60 c.c.) was treated with aluminium *iso*propoxide (4·5 g.), and the mixture heated under reflux for 4 hours. The reaction mixture was treated as described by Marker *et al.* (*loc. cit.*), and the product (10 g.) crystallised from dioxan–methyl alcohol, from which the ergosterol–*epi*ergosterol complex separated in needles, m. p. 196°. *Light absorption in alcohol* (Fig. 2): maxima, (a) 2815 A., log ε = 4·00; (b) 2720 A., log ε = 3·96. On standing for 2 days the complex had m. p. 155°, $[\alpha]_D^{20°}$ − 53·2° ($l$ = 1, $c$ = 0·6 in chloroform). A solution of the complex of either m. p. 196° or 155° (5 g.) in alcohol (90%; 200 c.c.) was treated with a solution of digitonin (20 g.) in alcohol (90%; 800 c.c.); and the mixture set aside overnight. The separated digitonide (10 g.) was taken up in hot pyridine (100 c.c.), and the solution treated with ether. The digitonin was removed by filtration, and the mother-liquor evaporated to dryness. Crystallisation of the residue from alcohol gave ergosterol (1·1 g.), m. p. 160°, $[\alpha]_D^{20°}$ − 127° ($l$ = 1, $c$ = 0·96 in chloroform), showing the characteristic absorption spectrum of ergosterol; the acetate, prepared in the usual manner, had m. p. 170°, $[\alpha]_D^{20°}$ − 90·1° ($l$ = 1, $c$ = 0·7 in chloroform). Neither the sterol nor its acetate depressed the m. p. of authentic ergosterol and its acetate respectively. The filtrate obtained after removal of ergosterol digitonide was worked up as described by Marker *et al.*, the trienol being obtained, after three crystallisations from acetone, in needles, m. p. 152°, $[\alpha]_D^{20°}$ + 41·3° ($l$ = 1, $c$ = 0·92 in chloroform). The acetate separated

from alcohol in plates, m. p. 126° (Marker *et al.* give m. p. 152°, $[\alpha]_D^{20°}$ + 50·0° for "*epi*ergosterol" and m. p. 126° for its acetate).

*Ergostatetraene* (VI).—The trienol (200 mg.), m. p. 152°, was heated under reflux with acetic anhydride (5 c.c.) and anhydrous sodium acetate (200 mg.) for 3 hours. On cooling, the *hydrocarbon* separated in plates, which after a single crystallisation from alcohol had m.p. 104°, $[\alpha]_D^{20°}$ − 40·5° ($l$ = 1, $c$ = 1·24 in chloroform) (Found : C, 88·6; H, 11·1. $C_{28}H_{42}$ requires C, 88·8; H, 11·2%). *Light absorption in alcohol* (Fig. 2) : maxima, (a) 3015 A.; (b) 3160 A., log ε = 4·28; (c) 3315 A.

*Lumistatrienone* (IV).—Lumisterol was oxidised by the method of Oppenauer (*loc. cit.*). After two crystallisations from light petroleum (b. p. 40—60°)–acetone (1 : 1) *lumistatrienone* separated in hard needles, m. p. 139—140°, $[\alpha]_D^{20°}$ + 48·7° ($l$ = 1, $c$ = 1·05 in chloroform) (Found : C, 85·1; H, 10·7. $C_{28}H_{42}O$ requires C, 85·2; H, 10·8%). *Light absorption in alcohol* (Fig. 3) : maximum, 2290 A., log ε = 4·23. The *semicarbazone* separated from methyl alcohol–chloroform in needles, m. p. 247° (decomp.) (Found : C, 77·2; H, 9·8; N, 9·05. $C_{29}H_{45}ON_3$ requires C, 77·05; H, 10·05; N, 9·3%).

*Reduction of Lumistatrienone : epiLumisterol.*—The reduction of lumistatrienone (10 g.) was effected by the method employed for ergostatrienone. After three crystallisations from acetone the lumisterol–*epi*lumisterol complex separated in needles, m. p. 159·5°, $[\alpha]_D^{20°}$ + 196·7° ($l$ = 1, $c$ = 0·6 in chloroform). Treatment of the complex (2 g.) with excess of digitonin in 90% alcohol gave *epi*lumisterol digitonide (4 g.), which on decomposition with pyridine gave epi*lumisterol* (0·9 g.); this separated from methyl alcohol in needles, m. p. 109—110°, $[\alpha]_D^{20°}$ + 224·6° ($l$ = 1, $c$ = 0·6 in chloroform) (Found : C, 84·9; H, 11·1. $C_{28}H_{44}O$ requires C, 84·8; H, 11·2%). *Light absorption in alcohol* (Fig. 3) : maximum, 2740 A., log ε = 3·98. The *acetate* separated from methyl alcohol in needles, m. p. 114—115°, $[\alpha]_D^{20°}$ + 175·0° ($l$ = 1, $c$ = 0·8 in chloroform) (Found : C, 82·2; H, 10·5. $C_{30}H_{46}O_2$ requires C, 82·1; H, 10·6%).

The filtrate obtained after removal of the digitonide was worked up as in the reduction of ergostatrienone, lumisterol being obtained, after two crystallisations from methyl alcohol, in needles, m. p. 116—117°, $[\alpha]_D^{20°}$ + 177·7° ($l$ = 1, $c$ = 1·1 in chloroform), showing the characteristic absorption spectrum of lumisterol; the acetate, prepared in the usual manner, had m. p. 99°, $[\alpha]_D^{20°}$ + 126·9° ($l$ = 1, $c$ = 0·4 in chloroform), and showed no depression in admixture with authentic lumisteryl acetate.

*Ergostatetraenone* (VII).—Dehydroergosterol was oxidised by the method of Oppenauer (*loc. cit.*). After five crystallisations from acetone *ergostatetraenone* separated in plates, m. p. 140—142°, $[\alpha]_D^{20°}$ + 190·0° ($l$ = 1, $c$ = 3·2 in chloroform) (Found : C, 85·75; H, 10·15. $C_{28}H_{40}O$ requires C, 85·65; H, 10·3%). *Light absorption in alcohol* (Fig. 4) : maximum, 2420 A., log ε = 4·50. The *semicarbazone* separated from methyl alcohol–chloroform in needles, m. p. 244° (decomp.) (Found : C, 77·6; H, 9·45; N, 9·0. $C_{29}H_{43}ON_3$ requires C, 77·45; H, 9·65; N, 9·35%).

*Reduction of Ergostatetraenone.*—The reduction of ergostatetraenone (1·1 g.) was effected by the method employed for ergostatrienone. After one crystallisation from dioxan–water the dehydroergosterol–*epi*dehydroergosterol complex crystallised in plates (0·8 g.), m. p. indefinite about 145°. *Light absorption in alcohol* (Fig. 4) : maxima, (a) 3200 A., log ε = 3·94; (b) 3400 A. Treatment of the complex with excess of digitonin in 90% alcohol gave dehydroergosterol digitonide (1·7 g.), which on decomposition with pyridine gave dehydroergosterol (0·35 g.); this separated from methyl alcohol in plates, m. p. 146°, $[\alpha]_D^{20°}$ + 148·3° ($l$ = 1, $c$ = 0·7 in chloroform). *Light absorption in alcohol* : maxima, (a) 3250 A., log ε = 4·045; (b) 3400 A.

*Ergostatrienone Enol-acetate* (VIII).—A solution of ergostatrienone (4 g.) in pyridine (10 c.c.) and acetic anhydride (10 c.c.) was heated under reflux for 3 hours. The solid separating on cooling was recrystallised from ethyl acetate–methyl alcohol (1 : 1), from which *ergostatrienone enol-acetate* separated in colourless plates (3·45 g.), m. p. 146°, $[\alpha]_D^{20°}$ − 143·5° ($l$ = 1, $c$ = 1·4 in chloroform) (Found : C, 82·8; H, 10·3. $C_{30}H_{44}O_2$ requires C, 82·6; H, 10·1%). *Light absorption in alcohol* (Fig. 1) : maxima, (a) 3010 A.; (b) 3165 A., log ε = 4·33; (c) 3310 A.

iso*Ergostatrienone* (IX).—*Ergostatrienone enol-acetate* (0·5 g.) was heated under reflux for 3 hours with a solution of potassium hydroxide (0·5 g.) in methyl alcohol (20 c.c.). The solid obtained by precipitation with water was recrystallised twice from methyl alcohol; *iso*ergostatrienone was thus obtained in colourless needles (0·4 g.), m. p. 108° alone and on admixture with a specimen prepared by the method of Wetter and Dimroth (*loc. cit.*); $[\alpha]_D^{20°}$ − 30·0° ($l$ = 1, $c$ = 1·2 in chloroform) (Found : C, 85·0; H, 10·8. Calc. for $C_{28}H_{42}O$ : C, 85·3; H, 10·7%). *Light absorption in alcohol* : maxima, (a) 2800 A., log ε = 4·52; (b) 3350 A. The semicarbazone

separated from methyl alcohol–chloroform in needles, m. p. 245—246° (decomp.) (Found: N, 9·45. Calc. for $C_{29}H_{45}ON_3$: N, 9·3%). *Light absorption in alcohol:* maximum, 3035 A., log ε = 4·67.

iso*Ergostatrienone Enol-acetate* (X).—*iso*Ergostatrienone (0·5 g.) in acetic anhydride (4 c.c.) and acetyl chloride (4 c.c.) was heated under reflux for 6 hours, the excess of acetyl chloride removed, and the solution allowed to cool. Recrystallisation of the separated solid from ethyl alcohol gave iso*ergostatrienone enol-acetate* in colourless needles (0·35 g.), m. p. 137°, $[\alpha]_D^{20°}$ – 84·6° ($l$ = 1, $c$ = 0·63 in chloroform) (Found: C, 82·5; H, 9·8. $C_{30}H_{44}O_2$ requires C, 82·9; H, 10·1%). *Light absorption in alcohol* (Fig. 1): maximum, 3040 A., log ε = 4·22.

*Ergostatetraenone Enol-acetate* (XI).—Ergostatetraenone (0·5 g.) was acetylated by the method employed for the preparation of the enol-acetate of ergostatrienone. *Ergostatetraenone enol-acetate* separated from ethyl acetate–methyl alcohol in flat needles (0·45 g.), m. p. 161°, $[\alpha]_D^{20°}$ – 232·5° ($l$ = 1, $c$ = 1·2 in chloroform) (Found: C, 82·8; H, 9·5. $C_{30}H_{42}O_2$ requires C, 82·95; H, 9·7%). *Light absorption in alcohol* (Fig. 1): maxima, (a) 3390 A.; (b) 3560 A., log ε = 4·24; (c) 3750 A.

*Lumistatrienone Enol-acetate* (VIII).—Lumistatrienone (5·4 g.) was acetylated by the method employed for the preparation of the enol-acetate of ergostatrienone. *Lumistatrienone enol-acetate* separated from ethyl acetate–methyl alcohol in colourless needles (4·3 g.), m. p. 98°, $[\alpha]_D^{20°}$ + 293·7° ($l$ = 1, $c$ = 1·2 in chloroform) (Found: C, 82·4; H, 9·8. $C_{30}H_{44}O_2$ requires C, 82·6; H, 10·1%). *Light absorption in alcohol* (Fig. 1): maximum, 3150 A., log ε = 4·28.

Our thanks are due to Imperial Chemical Industries Ltd. (Dyestuffs Group) for the award of a Scholarship which enabled one of us (G. S.) to participate in this investigation and to Dr. A. E. Gillam for the absorption spectra data.

THE UNIVERSITY, MANCHESTER. [*Received, April* 12*th*, 1938.]

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## 170. *The Preparation of Some* cis-*Azo-compounds.*

By A. H. COOK.

The isolation of *cis*-azobenzene by chromatographic analysis of an irradiated solution of the *trans*-form in petroleum on aluminium oxide is described. Other azo-compounds are shown to form unimolecular isomerides, to which is ascribed a *cis*-configuration. Those which have been isolated are relatively less stable than *cis*-azobenzene, but are separated from the normal form with remarkable ease on the chromatographic column. Attention is drawn to apparent marked differences in lability among closely related azo-compounds and to the insufficiency of existing conceptions and data to account for these differences.

G. S. HARTLEY has recently announced (*Nature*, 1937, **140**, 281; this vol., p. 633) the isolation of *cis*-azobenzene and the photometric detection of isomerides of some 4-substitued azobenzenes. The present communication on the preparation of several azo-compounds in the *cis*-form was deemed advisable while the work is still admittedly incomplete in order to avoid duplication of results.

The recognition of a *cis*-form of azobenzene analogous to maleic as compared with fumaric acid was, as in the work of Hartley, largely fortuitous and prompted by the observation that many azo-dyes, when submitted to chromatographic analysis, exhibit a serious departure from the normal chromatographic rule according to which a single compound should give only one adsorption band. This behaviour is not limited to azo-compounds, but is shown by dyes of other classes (Ruggli and Jensen, *Helv. Chim. Acta*, 1935, **18**, 624), anthocyanines (Karrer and Strong, *ibid.*, 1936, **19**, 25), etc., and must be generally ascribed at least in part to factors such as varying dispersion of the pigments as well as the possible presence of small amounts of isomeric compounds in the purest commercial dyes.

On investigating this abnormality more closely among the azo-compounds, however, it was noticed that some relatively complex representatives (*e. g.*, azophenols) were chromatographically homogeneous, but an old specimen of "purest" azobenzene, when

adsorbed on activated aluminium oxide from petroleum solution, gave a broad diffuse zone in the lower part of the column with a very narrow, sharply defined band of more strongly adsorbed material. The weakly adsorbed component, constituting the bulk of the azobenzene, behaved normally on being washed through the column and immediately readsorbed, giving only the single diffuse zone. The narrow band again appeared, however, if either the solution or the recovered solid was kept in ordinary diffuse light for a few days. By irradiating the solution before a mercury lamp, a considerable proportion of the initial azobenzene was converted, with darkening of the colour of the solution, into more strongly adsorbed material, which was eluted with petroleum-methanol and obtained at once as orange-red crystals, m. p. 71°, from cold petroleum. By performing the irradiation and chromatographic separation in absence of any considerable amounts of air it was shown that the phenomenon is associated only with irradiation and not with oxygenation (the presence of small amounts of azoxy-compounds has in the past led to unsubstantiated claims to have isolated isomeric azo-compounds; cf. H. Hartley and Stuart, J., 1914, **105**, 309). The new compound, which is identical (m. p. and mixed m. p.) with G. S. Hartley's *cis*-azobenzene prepared by a more tedious selective extraction procedure, is deeper in colour both in the solid and in the dissolved state than normal azobenzene, with which it gives large depressions in m. p. (mixed m. p. 35—45°), but reverts to the normal form very slowly at the ordinary temperature, more rapidly when fused, and partly when irradiated. [H. Hartley and Stuart (*loc. cit.*) and also C. V. and R. A. Gortner (*J. Amer. Chem. Soc.*, 1910, **32**, 1294) remark on the deep red colour of their supposed *cis*-isomeride, so it is possible that their product was substantially *cis*-azobenzene contaminated with oxygenated compounds.] Obviously an equilibrium is set up by irradiation, the chromatographic behaviour of normal and the new azobenzene being indistinguishable after a further period of irradiation. Cryoscopic molecular-weight determination in benzene showed the latter form to be unimolecular and therefore truly stereoisomeric with normal azobenzene. (Each of the *cis*-compounds described in this paper could be recovered unchanged when the solution in benzene was evaporated in a vacuum at room temperature after standing for moderate periods, so the possibility of the recorded molecular weights referring to re-formed *trans*-compound is excluded.) Both forms were catalytically reduced to hydrazobenzene, which was reoxidised to the normal form. Although the conditions and nature of the reduction made a quantitative comparison of the rates of reduction somewhat difficult, it seems that under the comparable conditions employed there is little difference between them. Addition compounds of azobenzene and other azo-compounds with polynitro-compounds (trinitrobenzene, trinitrotoluene, styphnic acid, with *cis*- and *trans*-azobenzene, benzeneazo-*p*-toluene, *pp'*-azotoluene, *p*-cyanoazobenzene, from alcoholic solution) did not prove suitable for characterising these stereoisomerides, nor did trustworthy evidence of their formation present itself (cf. Hoffmann and Kirmreuther, *Ber.*, 1910, **43**, 1767).

These early results suggested that the photochemical formation of *cis*-azo-compounds of considerable stability might be a general phenomenon, but at once anomalies appeared which only further work can explain. Thus with the combined irradiation–chromatographic technique a cis-*benzeneazo*-p-*toluene* (the *cis*-configuration in this and the other cases is assigned, in absence of physical evidence, by analogy with azobenzene and on the basis of molecular-weight determinations) was obtained resembling the lower homologue in its relation to the *trans*-isomer. Similarly *pp'*-azotoluene yielded a cis-pp'-*azotoluene*. In these instances and in all other cases where a *cis*-isomer which was sufficiently stable to be obtained substantially free from the *trans*-compound was observed, the solution became perceptibly darker on irradiation; the above substituted azobenzenes were markedly less stable in the *cis*-modification than the unsubstituted compound and readily reverted (in the case of *pp'*-azotoluene after only once melting at 100°) to the stable forms. With *oo'*- and *mm'*-azotoluenes neither the characteristic deepening in colour on irradiation nor the sharp separation of any isomeride on the chromatographic column could be observed and it seems clear that either *cis*-isomerisation does not take place or the isomeride is too labile to admit of isolation. Both of the above alkyl-substituted *cis*-azobenzenes were unimolecular in benzene solution, so simple polymorphism cannot account for the isomerism (cf. Schaum, Schaeling and Klausing, *Annalen*, 1916, **411**, 19[illegible] No evidence that benzene-

azo-α-naphthalene, αα'- or ββ'-azonaphthalene forms a stable *cis*-isomeride in the same way has yet been obtained.

A number of 4-substituted azobenzenes which are all presumably *trans* in configuration have been subjected to a preliminary examination of their ability to form *cis*-isomerides of sufficient stability to allow of their separation. 4-Hydroxy-, 4-acetoxy-, 4-amino- and 4-acetamido-azobenzenes, when irradiated in benzene or petroleum solution and subsequently chromatographically adsorbed on alumina, furnished some evidence, in the form of an indefinite " tailing " of the main zone or the development of subsidiary zones, of the transient formation of *cis*-isomerides, but in each case only the normal *trans*-modification was recovered. Alkylation of the *p*-hydroxyl group resulted in increased stability of the *cis*-modification, so that methyl and *ethyl* ethers of *cis*-*p*-benzeneazophenol could be obtained. Solidification of the pure *cis*-forms has not yet been effected, as reversion to the *trans*-forms is rapid and is complete within two days at the ordinary temperature in absence of light, the initially chromatographically homogeneous, deep red oils then solidifying to orange crystalline masses of the *trans*-compounds. *p*-Chloroazobenzene is rather more stable in the *cis*-form, but with substitution of cyanogen for the chlorine all stability apparently disappears and no *cis*-*p*-benzeneazobenzonitrile has been obtained.

It is clear that the possibility of intermediate quinonoid structures, which might account in part for the permanence of the *trans*-form in benzeneazophenol and *p*-aminoazobenzene, cannot explain the varying behaviour of other 4-substituted azobenzenes and azohydrocarbons.

The ease or impossibility of chromatographic separation of *cis-trans* azo-mixtures does not appear to be influenced to a practical extent by the nature of the aluminium oxide adsorbent. Mild deactivation by washing with water, removal of alkali by washing with phenol or acetic acid solution, or activation by treatment with lime-water (cf. Franck, *Arch. Pharm.*, 1937, 131) did not affect the properties of the separated *cis*-isomerides, although the amount of adsorbent necessarily varied. When adsorbents of even moderate activity were used, the separation from petroleum solution was always remarkably sharp in the sense that the whole of the *trans*-isomeride could usually be washed through the column while the *cis*-zone either remained stationary in the upper part of the column or moved only very slowly down. Chromatographic analysis thus seems to be generally applicable to the separation of *cis-trans* isomerides in the azo-series.

The isomerisation of β-carotene by alumina and the chromatographic isolation of the resulting ψ-α-carotene has been effected by Gillam and el Ridi (*Nature*, 1935, **136**, 914; *Biochem. J.*, 1936, **30**, 1735) and the detection of the spontaneous isomerisation of lycopene by its altered chromatogram was noted by Zechmeister and Tuzson (*Nature*, 1938, **141**, 249). In the polyene series the possibility of *cis-trans* isomerism about one or more ethylene linkages is accompanied by the possibility of transposition of the conjugated double bonds. However, there is clearly a similarity between the polyene isomerides and the nitrogenous compounds described in the present communication. It is noteworthy that, though the azo-compounds appear to yield more labile isomerides than olefins, the difference in adsorption affinity caused by the altered configuration of the aromatic nuclei about the azo-group is so great that chromatographic separations of *cis*- and *trans*-azo-compounds are probably at once the simplest and most complete separations of closely related compounds to be effected by this means.

Further work to investigate the generality of this phenomenon (*e. g.*, among azo-dyes) and the chemical properties of *cis*-azo-compounds, and to elucidate the factors influencing the lability of azo-compounds in this respect is in progress.

## Experimental.

All the following azo-compounds were purified chromatographically before irradiation by filtration of a dilute (1%) solution in light petroleum through Merck's " Aluminiumoxyd standardisiert nach Brockmann " and recovery of the azo-compound either directly from the filtrate or by elution of the main adsorption zone with petroleum containing 1% of methanol. The irradiation and chromatographic analysis were carried out in each case, except where otherwise stated, in an atmosphere of nitrogen.

cis-*Azobenzene*.—1 G. of *trans*-azobenzene in 50 c.c. of light petroleum was irradiated at a distance of 12—15″ from an unshielded quartz mercury vapour lamp for 30 minutes. The solution, which had become red, was filtered through a column (20 cm.; 2 cm. internal diameter) of Merck's alumina, which was then washed with 100 c.c. of petroleum. All unchanged *trans*-compound was washed through the column, but *cis*-azobenzene remained adsorbed in a very sharp zone 4 cm. in length, beginning at 1 cm. from the upper end of the column. The adsorbed material was eluted from this zone with 150 c.c. of light petroleum containing 1% of methanol, the petroleum filtered and, after removal of methanol by washing with water, dried over sodium sulphate and evaporated in a vacuum below 22°. The crystalline material obtained was recrystallised from a little cold petroleum, giving orange-red plates, m. p. 71°, mixed m. p. with *trans*-azobenzene, 35—45° (Found: C, 79·2; H, 5·65; N, 15·2; *M*, cryoscopic in benzene, 175. Calc. for $C_{12}H_{10}N_2$: C, 79·1; H, 5·5; N, 15·4%; *M*, 182).

*Reduction of* cis- *and* trans-*Azobenzenes*.—2·00 Mg. of platinum oxide (Adams's catalyst) were suspended in 1 c.c. of alcohol in a Barcroft respirometer so arranged that, when reduction of the catalyst was completed, 2·00 mg. of azobenzene could be brought into contact with the catalyst and reduced. The compensating flask of the apparatus was charged in the same way except that the azobenzene was omitted. The results show that there is no very considerable difference under these conditions in the rates of hydrogenation of the isomers and that reduction proceeds beyond the hydrazo-stage, although there is no difficulty in recognising the completion of the primary rapid reduction.

2·00 Mg. of azo-compound in 0·5 c.c. of alcohol + 2·00 mg. of Adams's catalyst suspended in 1 c.c. of alcohol. Temp. 20°.

| Time, mins. | | 1 | 2 | 3 | 4 | 5 | 6 | 8 |
|---|---|---|---|---|---|---|---|---|
| Uptake of H, c.mm. at *N.T.P.* | *cis*- | 146 | 189 | 209 | 237 | — | 268 | 330 |
| | *trans*- | 135 | 250 | 308 | — | 370 | 410 | — |

The initial slightly more rapid reduction of the *trans*-isomeride was repeatedly confirmed when the compensating flask of the respirometer contained the second modification. The colourless solutions were filtered after the theoretical volume of hydrogen had been absorbed (246 c.mm.), washed with water, oxidised with air, and extracted with petroleum; the azo-compounds thus obtained were chromatographically indistinguishable from normal *trans*-azobenzene.

cis-*Benzeneazo*-p-*toluene*.—A solution of 0·5 g. of benzeneazo-*p*-toluene in 25 c.c. of petroleum was irradiated at a distance of 12″ from a quartz mercury vapour lamp for 3 hours and filtered through a column of alumina (20 cm.; 1·7 cm. diameter), and the chromatogram washed with 50 c.c. of petroleum. The whole of the unchanged azo-compound passed into the filtrate, leaving the *cis*-compound adsorbed as a layer, 3 cm. long, at the top of the column. The zone was removed, and the remainder of the column used to rechromatograph the solution after it had been concentrated to 25 c.c. and again irradiated for 2 hours. The "cis"-zones were united and worked up as for *cis*-azobenzene. The residue obtained on evaporation was oily, but crystallised, when rubbed, to a deep red solid (m. p. 40°), which had m. p. 42—45° after rapid crystallisation from methanol–water at a low temperature. Yield, 110 mg. (Found: N, 14·4; *M*, cryoscopic in benzene, 181. $C_{13}H_{12}N_2$ requires N, 14·3%; *M*, 196).

*Azotoluenes*.—*oo*′-Azotoluene was prepared by Vorländer and Meyer's method (*Annalen*, 1901, **220**, 122) (b. p. 210°/5 mm.; recrystallised from alcohol, red prisms, m. p. 55°; yield, 37%), but was more conveniently obtained from *o*-nitrotoluene by the method used for the preparation of *pp*′-azotoluene (yield, 52%). It gave no indication of the ready formation of a stable *cis*-modification.

Long irradiation of the *mm*′-isomer in air gave a small amount of a product, which separated on the chromatographic column as a firmly adsorbed, yellow compound. Elution in the usual way gave stable, long yellow needles, m. p. 59° (from petroleum). The *compound* has the composition of an azoxytoluene, but does not appear to be identical with any of those hitherto known (Found: C, 74·0; H, 6·3; N, 12·45. $C_{14}H_{14}ON_2$ requires C, 74·4; H, 6·25; N, 12·4%). Distillation with iron filings gave a red oil, which soon solidified and after filtering in petroleum solution through a short column of alumina yielded *mm*′-azotoluene, m. p. and mixed m. p. 54°. It is not impossible that the new compound is a (*cis*) stereoisomeride of that hitherto known (m. p. 39°), but it is significant that it has not yet proved possible to convert the new compound into the old. *pp*′-Azotoluene was prepared by the following method: A milky suspension of 90 g. of stannous chloride (dihydrate) in 150 c.c. of water was added slowly, so

that the temperature did not exceed 60°, with stirring to 64 g. of sodium hydroxide in 250 c.c. of water. The sodium stannite solution was boiled, 27 g. of *p*-nitrotoluene in 100 c.c. of alcohol added, and the whole shaken. *pp'*-Azotoluene separated in bright orange crystals, which were collected hot after 30 minutes' refluxing and recrystallised from alcohol; m. p. 145°. Yield, 18 g. (85%).

cis-pp'-*Azotoluene*.—A solution of 400 mg. of the *trans*-compound in 100 c.c. of light petroleum was irradiated at a distance of 12" from a mercury lamp for 30 minutes and then chromatographed on a column of Merck's alumina (20 cm., 2 cm. diameter). The *trans*-compound was completely washed through the column with 120—150 c.c. of petroleum. cis-pp'-*Azotoluene* remained adsorbed as a layer 1·5—2 cm. long, beginning 1 cm. from the top of the column. Isolation as for *cis*-azobenzene and crystallisation at 0° from a little petroleum yielded 30 mg. of deep red needles, m. p. 105° (rapid heating), mixed m. p. with the *trans*-compound, 95—100° (Found: C, 79·8; H, 6·55; *M*, cryoscopic in benzene, 220. $C_{14}H_{14}N_2$ requires C, 80·0; H, 6·7%; *M*, 210). After melting, the substance solidified as pure *trans*-azotoluene, m. p. 144°.

p-*Benzeneazophenol*.—Adsorption even on mildly deactivated alumina was too firm from petroleum solution and unsatisfactory from benzene solution. 500 Mg., dissolved in 50 c.c. of benzene, were adsorbed on alumina (25 cm.; 1·7 cm. diameter) and the broad band extending 7 cm. from the top of the column was developed with 50 c.c. of benzene and then with 50 c.c. of benzene + 10 c.c. of alcohol. 300 Mg. of the azo-compound were thus recovered from the filtrate; the remainder stained the whole of the column a uniform orange-yellow colour and was only eluted with alcoholic ammonia. After irradiation of the chromatographically pure product (300 mg. in 50 c.c. of benzene; irradiated for 30 mins. at 12" from the mercury lamp) an orange band, which was distinct from the main, more easily eluted, unchanged azo-compound, was developed on washing the column with ether, but in each case only normal *trans*-benzeneazophenol was recovered. *p*-Benzeneazophenyl acetate behaved similarly, as did also 2 : 4-bisbenzeneazophenol and its acetate.

p-*Aminoazobenzene*.—Purification of the crude product was best effected by running a 1% solution in benzene through a column of alumina and concentrating the filtrate until *p*-aminoazobenzene crystallised (8—10 g. can be treated on a column of Merck's alumina, 20 cm.; 2 cm. diameter). No isomerisation was chromatographically detectable after a 1% solution of benzene had been irradiated for 3 hours at a distance of 12" from the mercury lamp. Acetamidoazobenzene behaved similarly and furnished no evidence of a stable *cis*-isomeride.

p-*Benzeneazophenetole*.—500 Mg., dissolved in 100 c.c. of petroleum, were irradiated and chromatographed. An upper zone (3—4 cm.) of firmly adsorbed material was developed and eluted with 200 c.c. of 1% methanol in petroleum. A deep red oil (55 mg.) was obtained in the usual way (Found: C, 74·3; H, 6·1. $C_{14}H_{14}ON_2$ requires C, 74·4; H, 6·25%). The material became lighter in colour during 2 days and solidified to normal benzeneazophenetole, m. p. 78—79°.

p-*Chloroazobenzene*.—The following modified preparation was found convenient: 25 g. of aminoazobenzene hydrochloride in 700 c.c. of water and 77 c.c. of concentrated hydrochloric acid were diazotised with 7 g. of sodium nitrite in 35 c.c. of water. After 30 minutes the filtered solution was poured into a boiling solution of 14 g. of cuprous chloride in 125 c.c. of concentrated hydrochloric acid and again filtered after 10 minutes. The grey-black mass was washed with hydrochloric acid, caustic soda solution, and water and a benzene extract (150 c.c.) of the residue was filtered through two columns of Merck's alumina. The recovered compound was redissolved in 100 c.c. of warm petroleum, filtered again through an alumina column (25 cm.; 2·5 cm. diameter), and the filtrate concentrated until deep orange needles, m. p. 88—90°, crystallised (yield, 8 g.; 21%) (cf. Mentha and Heumann, *Ber.*, 1886, **19**, 3022).

500 Mg. of the chromatographically pure product in 100 c.c. of petroleum were irradiated for 30 minutes and then chromatographed, the column (20 cm.; 2 cm. diameter; Merck's alumina) being washed with 50 c.c. of petroleum. The zone of *cis*-compound was 2—3 cm. long, beginning 1 cm. from the top of the column. The products of several separations (each *ca.* 30—50 mg.) were worked up together in the usual way. Only a deep red oil was obtained, which solidified after 2 days to *trans*-*p*-chloroazobenzene (Found: C, 66·85; H, 4·1. Calc. for $C_{12}H_9N_2Cl$: C, 66·6; H, 4·2%).

p-*Cyanoazobenzene*.—A diazotised solution of 35 g. of aminoazobenzene was added to potassium cuprocyanide soution at 90° (88 g. of copper sulphate in 400 c.c. of water at 90°, treated with 98 g. of potassium cyanide in 100 c.c. of water). The crude product was collected when cold, washed, and dried on a tile. A benzene extract of the residue (200 c.c.) was passed

through three columns of alumina (20 cm.; 2 cm. diameter); the crystalline residue obtained from the filtrate sublimed in a vacuum in pale orange needles, m. p. 120·5°.

Prolonged irradiation in petroleum solution, and chromatographic analysis of the resulting solution gave no indication of isomerisation beyond a tail to the main chromatographic zone which quickly followed the bulk of adsorbed material on development.

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## 171. *A Criterion for the Mechanism of the Reaction between Alkyl Halides and Hydroxylic Solvents. Reactions of* tert.*-Butyl Chloride.*

By LESLIE C. BATEMAN, EDWARD D. HUGHES, and CHRISTOPHER K. INGOLD.

A means of distinction between the two mechanisms of nucleophilic aliphatic substitution, suitable for application to those first-order reactions in which the reagent is in large excess, is based on the circumstance that in bimolecular substitution the product is determined in a reaction whose rate can be measured, whilst in unimolecular substitution it is formed, not in the rate-measured process, but in a subsequent fast reaction:

$$Y + R\vdots\!-X \longrightarrow Y-R + X \quad . \quad . \quad . \quad \text{(Bimolecular)}$$

$$\left.\begin{array}{l} R\vdots\!-X \longrightarrow R^+ + X \text{ (slow)} \\ Y + R^+ \longrightarrow Y-R \text{ (fast)} \end{array}\right\} \quad . \quad . \quad \text{(Unimolecular)}$$

Olson and Halford having advanced a successful quasi-thermodynamic expression for the interpolation of reaction rates in binary solvent mixtures from observed rates in two mixtures of different composition, we can apply the principle stated as follows. Consider the simultaneous hydrolysis and alcoholysis of an alkyl halide in aqueous alcohol. Whatever may be the mechanism, the two constants that can be derived from rate measurements at two solvent compositions will permit calculation of the rate at some other solvent composition. If the mechanism is bimolecular, the same two rate-derived constants will also allow calculation of the composition of the substitution product (alcohol plus ether), because this is formed in the reaction whose rate we measure; whereas if the mechanism is unimolecular, the measured rates will have no connexion with the composition of the product, which is formed in a different reaction-stage. Thus by determining both rates and product compositions we can discover the mechanism. This criterion has been applied to the hydrolysis and methyl- and ethyl-alcoholysis of *tert.*-butyl chloride. Despite the excellence of the rate interpolations, the product compositions are widely different from those calculated by Olson and Halford's formula on the assumption that the mechanism is bimolecular. It is concluded that the mechanism is unimolecular, in agreement with other evidence.

The four methods now available for the solving of such problems are summarised, and their limitations are noted.

THE theory of aliphatic substitution sketched by Ingold and Rothstein (J., 1928, 1217; cf. Ingold and Patel, *J. Indian Chem. Soc.*, 1930, **7**, 95) and generalised by Hughes, Ingold, and Patel (J., 1933, 526) and Hughes and Ingold (J., 1935, 244) recognises two main classes of substitution, determined by the electrical affinities of the reagent, two divisions within each class, depending on whether one or two bonds are exchanged, and, for every one of these kinds of substitution in solution, two typical mechanisms, one involving replacement in a single stage and the other preliminary ionic fission. This paper is a contribution to the problem of distinguishing between these mechanisms.

*The method to be considered is in principle* general, but we shall confine explicit discussion to substitutions by nucleophilic reagents which effect an exchange of one bond. The first mechanism, termed "bimolecular," may then be formulated

$$Y + R\vdots\!-X \longrightarrow Y-R + X \quad . \quad . \quad . \quad . \quad . \quad (S_N2)$$

where the charges on Y and X are unspecified, being subject only to the restrictions im-

posed by the electron transfer from Y to R and from R to X. The reaction is normally of the second order, and may be of the first order, *e.g.*, if the reagent Y is in very large excess. The second mechanism, which we term "unimolecular," may be expressed

$$\left.\begin{array}{l} R—X \longrightarrow R^+ + X \text{ (slow)} \\ Y + R^+ \longrightarrow Y—R \text{ (rapid)} \end{array}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (S_N1)$$

where the electron transfers are as before. Here the separation of bond-fission and bond-formation into stages, of which the former controls the rate, causes the reaction to exhibit first-order kinetics, independently of the relative concentrations of the reagents. We have emphasised (cf. Hughes and Ingold, *loc. cit.*) that the solvent must play an especially important part in the ionic fission, since in all spontaneous ionisations it is solvation which reduces the activation energy to accessible values; and, furthermore, that the transition from one mechanism to the other cannot be absolutely sharp, as there must be degrees of time-separation between the bond-breaking and bond-forming processes (cf. Hughes, Ingold, and Patel, *loc. cit.*; Gleave, Hughes, and Ingold, J., **1935**, 236; Hughes, Ingold, and Shapiro, J., **1936**, 225).

When the entering substituent comes from a reagent present in small and controllable concentration there is usually no difficulty in distinguishing these mechanisms kinetically. Thus, kinetic data show that the action of halide ions on α-phenylethyl halides is bimolecular in acetone and unimolecular in sulphur dioxide, whilst the attack of halide ions on alkyl-sulphonium ions is unimolecular even in acetone. Since these examples of kinetically established unimolecular reactions were recalled (Hughes and Ingold, *loc. cit.*), others have arisen in the action of water and chloroacetate ions on *tert.*-butyl chloride in formic acid as solvent, and of halide ions, water, and amines on benzhydryl halides in sulphur dioxide (Bateman and Hughes, J., **1937**, 1187, and unpublished work).*

There is, however, an important class of examples, *e.g.*, the hydrolysis of alkyl halides in aqueous solvents, in which the entrant group may come from a relatively large quantity of the solvent. For these reactions, kinetics are not determinative; and other criteria of mechanism have been advanced. For example, we have concluded that the water-hydrolysis of α-bromopropionic acid (molecules) is bimolecular, whilst that of *tert.*-butyl chloride is unimolecular, but not on kinetic grounds, as both reactions are of the first order. We shall summarise the available methods of making such decisions after having illustrated a new method, which, we think, has considerable potential importance.

This method arises as an extension of an attempt by Olson and Halford (*J. Amer. Chem. Soc.*, 1937, **59**, 2644) to solve the same problem. The example is the simultaneous hydrolysis and alcoholysis of *tert.*-butyl chloride in aqueous-alcoholic solvents. This total first-order reaction was originally examined by Hughes (J., 1935, 255), who found that the rate was unaffected by hydroxonium or by hydroxide ions, and increased with the ionising power of the solvent, *e.g.*, with an increase in the water content of aqueous alcohol. Hughes concluded that the reaction was unimolecular.

With reference to the effect of such variations of solvent composition, Olson and Halford considered the consequence of supposing the reaction to be bimolecular. First, they set up the rate equation

$$\text{Rate} = (k_a p_a + k_w p_w) p_{RCl}$$

where $k_a$ and $k_w$ are specific rate constants for pure alcohol and pure water, and $p_a$ and $p_w$ are the partial vapour pressures of these constituents of the solvent mixtures, $p_{RCl}$ being the partial vapour pressure of the *tert.*-butyl chloride. From observed rates at two extremes of solvent composition, the constants, $k_a$ and $k_w$, were obtained; and these were then used in order to interpolate for rates at intermediate solvent compositions. Furthermore, from the assumptions made it followed that the two terms $k_a p_a p_{RCl}$ and $k_w p_w p_{RCl}$ respectively represent the rates of formation of *tert.*-butyl alkyl ether and *tert.*-butyl alcohol; so that the authors were able also to calculate the composition of the reaction product corresponding to each solvent mixture. Using Hughes's rate data for mixtures of ethyl

* W. Taylor's conclusions in this field will be discussed in a forthcoming criticism.

alcohol and water, and new results of their own for mixtures of methyl alcohol and water, they showed that the rate-interpolation formula worked extremely well. They therefore concluded that the reaction was bimolecular.

It is, however, questionable whether any conclusions at all should be drawn at that stage of the investigation. Olson and Halford did not consider how the theoretical consequences of the unimolecular mechanism compare and contrast with those of its alternative, and they did not attempt to ascertain whether their calculated compositions of the reaction product agreed with experiment. This, as we shall show, is the crucial point.

The rate formula given depends on the idea that the transition state of reaction constitutes a mode of escape (in the thermodynamic sense) for all participating entities, whose tendency to form a transition state is thus likely to be closely correlated with other measures of fugacity, *e.g.*, vapour pressure. Although it is not altogether clear that Olson and Halford's treatment of the transition state is formally correct, we should certainly expect a rate-interpolation formula based on a mixture law for the fugacities of the solvent components to have much better success than any similar function of concentrations, at least where there is any marked lack of proportionality between fugacity and concentration. But this holds generally for reactions in solution, inasmuch as the solvent always enters into the transition state of such reactions. It holds *inter alia* for the slow stage of the unimolecular mechanism, and, since the measured reaction rate is the rate of this stage, the constants $k_a$ and $k_w$ that we can obtain from observed rates should enable to us calculate the dependence of the rate of the slow stage, *i.e.*, of the experimental rate, on the solvent composition. On the other hand, it is characteristic of the unimolecular mechanism that the products (in our case the butyl alcohol and butyl alkyl ether) are not determined in the reaction stage whose rate is measured : they are formed in subsequent fast reactions, which may also be subject to rate laws expressible in terms of fugacities, although the specific constants involved are experimentally inaccessible; it is from *these* constants, if we knew them, that we might be able to calculate the composition of the reaction product, not from the constants found kinetically. Therefore the essential thing to do in order to obtain a distinction between the two mechanisms is to ascertain whether the measured specific rate constants that are successful in the rate interpolation hold also for the calculation of the composition of the product. If they do, and do so consistently, then that indicates that the products are formed in the reaction stage whose rate is measured; and if they do not, then it shows that the products are formed otherwise than in the rate-measured stage. Only with such evidence should we feel justified in concluding in the former case that the reaction is bimolecular, and in the latter that it is unimolecular.

We are able to supply the required data for the hydrolysis and alcoholysis of *tert.*-butyl chloride. Using three mixtures of ethyl alcohol and water and three of methyl alcohol and water, for each of which Olson and Halford calculated the proportion of *tert.*-butyl alkyl ether that should be formed if the reaction is bimolecular, we have experimentally determined the proportion in which ether is formed. We have, of course, ascertained that, under the conditions used, there is no interconversiou of products once they are formed. The actual products are *tert.*-butyl ethyl or methyl ether, *tert.*-butyl alcohol, and *iso*butylene. The last we have regarded as material side-tracked from the substitution processes, but the proportions are rather small and therefore it makes no great difference whether or not we include it amongst the products on the basis of which the percentage of ether is expressed. The results are in Table I, from which it will be seen that the observed proportions of ether are far larger (2—3 times) than the proportions calculated by Olson and Halford from rate data. The differences are very much greater than the errors inherent either in the experiments or in the calculations. We conclude that the substitution products are formed otherwise than in the reaction stage whose rate is observed. Therefore, by this as by previous tests, the reaction is essentially unimolecular.

For convenience we summarise the four chief methods now available for the diagnosis of reaction mechanism in those first-order substitutions in which the direct kinetic method is unavailable on account of the fact that the entrant group is derived from a large quantity of solvent. We note also the principal limitations associated with each method.

TABLE I.

*Composition of Products of Reaction of* tert.-*Butyl Chloride with Aqueous-alcoholic Solvents at* 25°, *and Comparison with Olson and Halford's Theoretical Values.*

| | Composition of solvent. (mols. %). | | Composition of product. (mols. %). | | | $\frac{100 \times \text{Ether}}{\text{Alcohol} + \text{Ether}}$ | |
|---|---|---|---|---|---|---|---|
| Solvent. | ROH. | $H_2O$. | Olefin. | Ether. | Alcohol.* | Calc.† | Found. |
| EtOH + $H_2O$ | 31·7 | 68·3 | *ca.* 13 [a] | 15·5 | 71·5 | 8 | 18 |
| | 55·3 | 44·7 | 17 [b] | 27 | 56 | 11 | 33 |
| | 73·6 | 26·4 | *ca.* 22 [c] | 41 | 37 | 18 | 53 |
| MeCH + $H_2O$ | 51·0 | 49·0 | 9 | 36 | 55 | 17 | 40 |
| | 71·6 | 28·4 | 13 | 59 | 28 | 29 | 68 |
| | 83·6 | 16·4 | *ca.* 18 [d] | 68 | 14 | 43 | 83 |

* By difference. † Calculations by Olson and Halford (*loc. cit.*).

[a] Approximately estimated by multiplying the following olefin figure (*b*) by the ratio of the proportions in which olefin is formed from *tert.*-amyl chloride in solvents having the compositions of the first two in the table (Hughes and MacNulty, J., 1937, 1283).

[b] Cooper, Hughes, and Ingold, J., 1937, 1280.

[c] Approximately estimated from the previous olefin figure (*b*) by means of considerations similar to those explained above (*a*).

[d] Approximately estimated from two previous olefin figures as explained.

(1) The first depends on the large effects arising from changes of structure in the *compound substituted on the rate of reaction*; for, in agreement with Evans and Polanyi (*Trans. Faraday Soc.*, 1936, **32**, 1333), we regard the logarithm of the rate as a more useful index than the Arrhenius critical energy as usually determined, though either can be used when the differences are sufficiently great. In substitution by nucleophilic reagents, electron accession to the seat of substitution decelerates the bimolecular reaction, provided the mechanism is well removed from bimolecular–unimolecular transition, and it strongly accelerates the unimolecular reaction universally. Whether or not a substitution is well removed from transition can usually be discovered by examination of an extended range of structures (papers of Hughes or Ingold cited; cf. Hughes, *Trans. Faraday Soc.*, 1938, **34**, 185; further examples in most other papers of this series).

(2) The second method utilises the effect on reaction rate of changes in the reagent, and especially on the action, or absence of action, of reagents which are much more strongly acidic or basic than the solvent. If vastly more powerful reagents than the solvent do not influence the rate, we conclude that such reagents are unable to affect the form of the main energy barrier; and therefore that they, and *a fortiori* the solvent itself, give up the entrant group after this main barrier has been passed. If, on the contrary, such strong reagents do affect the rate, then that means that in their presence a bimolecular reaction occurs; but it remains an open question, so far as this test is concerned, whether or not the same is true for the reaction with the solvent (Hughes and Ingold, *loc. cit.*).

(3) This is the method now illustrated, which employs the effect of solvent variation. Cases have been noted (*idem, ibid.*) in which we expect, and find, qualitatively opposite effects of solvent changes on the rates of bimolecular and unimolecular substitutions; but in all these cases an ionic reagent is involved, whose concentration can be controlled, so that they do not belong to the present problem. Just the same is true of effects (Cowdrey, Hughes, and Ingold, J., 1937, 1208) arising from the addition of neutral salts. Thus the method of solvent variation first becomes generally useful with the present development, to which the way was prepared by Olson and Halford.*

(4) Finally, there is the stereochemical method, limited, of course, to substitutions at an asymmetric centre. No outline need be given, as the matter has recently been fully discussed (Hughes, Ingold, and others, J., 1937, 1196, *et seq.*; Hughes, *Trans. Faraday Soc.*, 1938, **34**, 202).

These methods are just as available when the direct kinetic method can also be em-

* The method is more useful than yet appears, because a second general criterion of mechanism, which will be explained and applied later, can be based on Olson and Halford's valuable work.

ployed; but their value is naturally greater when the reaction order fails to give the information.

## EXPERIMENTAL.

*Materials.*—*tert.*-Butyl chloride of the quality used formerly (J., 1935, 255) had b. p. 50·6—50·8°/766 mm. Absolute ethyl and methyl alcohols were purified and fully dried by Lund and Bjerrum's method (*Ber.*, 1931, **64**, 210). Aqueous mixtures are specified by volume, *e.g.*, "60%-EtOH" means the mixture made from 6 vols. of ethyl alcohol and 4 vols. of water. Ethyl *tert.*-butyl ether, prepared by heating *tert.*-butyl bromide with ethyl alcohol, with periodic neutralisation by means of ethyl-alcoholic sodium ethoxide, was well washed with water, dried, and distilled once from barium oxide and twice from potassium; it then had b. p. 71·5—72°/746 mm. Methyl *tert.*-butyl ether, prepared similarly, had b. p. 55—56°/769 mm.

*Estimation of* tert.*-Butyl Ethyl and Methyl Ethers in Reaction Mixtures from* tert.*-Butyl Chloride and Aqueous Ethyl and Methyl Alcohols.*—The physical properties of the constituents of the reaction mixtures render the quantitative isolation of these ethers difficult. Extraction with solvents proved unsatisfactory. The method adopted, which we claim to give reliable estimates of the ethers, was first to carry out an "isolation experiment" in which the reaction mixture was fractionated after dilution with water and the ether was isolated as described below for a typical case; and then to proceed with a parallel "recovery experiment" on a synthetic solution corresponding in all respects to the completed reaction mixture, except for the omission of olefin, which in any case escapes from unsealed vessels. Although there were minor variations of procedure in the different isolations, each recovery experiment was carried out *exactly* like the corresponding isolation experiment. It was found possible to recover 61—67% of the ether in a state of complete purity. Further experiments with synthetic solutions showed that this degree of uniformity in the recovery obtained over a considerably wider range of ether concentrations than actually arose in the isolation experiments, holding, to quote the extreme examples, for synthetic solutions containing the equivalent of as little as 1·6%, or as much as 100%, of ether. (The lowest and the highest estimate of ether in the isolation experiments were 15·5% and 68%.)

Isolation and recovery experiments were carried out with the following media: "60%-," "80%-," and "90%-EtOH," and "70%-," "85%-," and "92%-MeOH." For the isolation experiments in "90%-EtOH" and "92%-MeOH," 25 c.c. of *tert.*-butyl chloride were dissolved in the medium, a few drops of phenolphthalein added, and the whole was made up to 500 c.c. For "85%-MeOH" the quantities were 40 c.c. of the chloride made up finally to 800 c.c.; whilst for the other media they were 50 c.c. of the chloride made up to 1000 c.c. The mixtures, kept in stoppered bottles in a thermostat at 25·0° ± 0·02°, were maintained nearly neutral by running in as necessary a solution of sodium hydroxide in the appropriate medium. This was intended as a precaution against any interconversion of products, which does under some conditions take place in acid media. We showed, however, by blank isolation and recovery experiments, in the former of which different proportions of *tert.*-butyl alcohol and *tert.*-butyl alkyl ether, in particular, pure *tert.*-butyl alcohol, replaced the *tert.*-butyl chloride, that the alcohol and ether undergo no trace of interconversion even under much more acidic conditions than obtained in the experiments summarised. We already knew from previous work (Cooper, Hughes, and Ingold, *loc. cit.*; Hughes and MacNulty, *loc. cit.*) that there could be no interconversion between *iso*butylene on the one hand and *tert.*-butyl alcohol and its alkyl ether on the other under the conditions employed.

In all the experiments with *tert.*-butyl chloride, its initial concentration was 0·45M.; its hydrolysis and alcoholysis would therefore change the concentrations of the solvent components by amounts of that order of magnitude. The neutralisation will produce a further change of comparable magnitude but in the opposite direction. As the most dilute solvent component in any of the mixtures (the water in the "92%-MeOH") was of concentration 16M., all solvent compositions may be regarded as sufficiently constant throughout reaction for the purposes of the comparison of Table I.

In illustration of the experimental method we now give details of the isolation of methyl *tert.*-butyl ether from the reaction product formed in "85%-MeOH." The reaction mixture, after dilution with water (500 c.c.), was distilled with an 8-pear column to give the following fractions: (1*a*) 13 c.c., b. p. 51—65°; (1*b*) 20 c.c., b. p. 65—70°; (1*c*) 20 c.c., b. p. 70—71·6°; (1*d*) 80 c.c., b. p. 71·6—73°. With water (6 c.c.), 1*a* gave an upper layer, which was washed with water, whilst 1*b*, 1*c*, and 1*d* gave no separation of layers. Fractions 1*b* and 1*c*, water, and the washings from 1*a*, were combined and distilled: (2*a*) 13 c.c., b. p. up to 64°; (2*b*) 6 c.c

b. p. 64—82°. With water, 2*a* gave an upper layer, which was washed with water, whilst 2*b* gave no separation. Fraction 1*d* together with water was distilled : (3*a*) 2 c.c., b. p. up to 64°; (3*b*) 8 c.c., b. p. 64—75°. Water produced no separation of layers with either fraction. All washings and fractions which gave no separation with water were now combined, and, with added water, distilled : (4*a*) 6 c.c., b. p. up to 64°; (4*b*) 4 c.c., b. p. 64—80°. With water, 4*a* gave a top layer, which was washed with water, whilst 4*b* gave no separation. The washings from 4*a*, together with 4*b* and added water, were distilled : (5*a*) 2 c.c., b. p. up to 70°. Addition of water and calcium chloride gave an upper layer. The top layers (crude ether) from 1*a* (6 c.c.), 2*a* (9 c.c.), 4*a* (3 c.c.), and 5*a* (1 c.c.) totalled 19·0 c.c. A portion (9·8 c.c.) of this was subjected to the following distillations : (i) From fused barium oxide : yield 9·2 c.c., b. p. 52—56°. (ii) From potassium : yield 8·5 c.c., b. p. 54—56°. (iii) From potassium : yield 7·9 c.c., b. p. 55—56° (Found : C, 67·5; H, 13·6. Calc. for $C_4H_9{\cdot}O{\cdot}CH_3$ : C, 68·2; H, 13·6%. *Note* : The analyses for methyl ethers were all slightly low for carbon, and this was not rectified by further distillation.) The over-all yield is thus 19·0 × 7·9/9·2 = 16·3 c.c.

The corresponding recovery experiment was carried out with the following solution : 960 c.c. of " 85%-MeOH " (the excess of this over the amount used to make up the *tert.*-butyl chloride to 800 c.c. in the isolation experiment being equal to the volume of the alkali solution added), 21 g. of sodium chloride, 8 g. of *tert.*-butyl alcohol, a few drops of phenolphthalein solution, a few drops of a solution of sodium hydroxide in " 85%-MeOH," and 25·0 c.c. of methyl *tert.*-butyl ether. By an identical isolation process, 19·7 c.c. of crude ether were recovered, which by the above three-stage rectification process gave 15·3 c.c. of the pure ether.

Numerical particulars of the whole series of experiments are summarised in Table II. All yields quoted are those of material fully rectified as above described, and analysed.

TABLE II.

*Estimations of* tert.*-Butyl Methyl and Ethyl Ethers.*

| Medium. | $H_2O$ content, mols. %. | Initial $Bu^{\gamma}Cl$. G. | Vol. (c.c.) of solution. Initial. | Final. | Pure ether isolated. G. | Mols. %. | Analyses of ether,* %. C. | H. | Percentage recovery (by expt.). | Ether formed † (mols. %). |
|---|---|---|---|---|---|---|---|---|---|---|
| 60%-EtOH | 68·3 | 42·0 | 1000 | 1150 | 4·7 | 10·2 | 70·5 | 13·5 | 65·5 | 15·5 |
| 80%- ,, | 44·7 | 42·0 | 1000 | 1200 | 7·5 | 16·2 | 70·6 | 13·7 | 60·6 | 26·7 |
| 90%- ,, | 26·4 | 21·0 | 500 | 700 | 6·35 | 27·3 | 70·2 | 13·8 | 67·2 | 40·6 |
| 70%-MeOH | 49·0 | 42·0 | 1000 | 1200 | 8·8 | 22·1 | 67·6 | 13·3 | 61·2 | 36·0 |
| 85%- ,, | 28·4 | 33·6 | 800 | 1000 | 11·6 | 36·3 | 67·5 | 13·6 | 61·2 | 59·3 |
| 92%- ,, | 16·4 | 21·0 | 500 | 700 | 8·6 | 43·0 | 67·5 | 13·6 | 62·9 | 68·4 |

* Calc. for $Bu^{\gamma}OEt$ : C, 70·6; H, 13·7%. Calc. for $Bu^{\gamma}OMe$ : C, 68·2; H, 13·6%.

† These estimates are believed to be correct to about ±4% of the figures listed.

*Estimation of* iso*Butylene formed from* tert.*-Butyl Chloride and Aqueous Alcohol.*—Estimations were carried out in " 70%-MeOH " and " 85%-MeOH." It was necessary to steer between two possible disturbances (Cooper, Hughes, and Ingold, *loc. cit.*; Hughes and MacNulty, *loc. cit.*). One is that, in a solution which is allowed to become too strongly acid, the olefin after being formed slowly disappears by adding on the solvent. The other is that in strongly alkaline solution there is a small incursion of bimolecular olefin formation, *i.e.*, elimination of hydrogen chloride by direct attack of hydroxide or methoxide ions; this increases the proportion of olefin formed above the value characteristic of weakly alkaline or acidic solutions. Between the limits thus imposed there is a wide " safe " region, and for convenience we have used the region between 0·1N-alkali and the neutral point, solutions originally of about the alkalinity stated being allowed to run nearly neutral.

The method was as follows. Sodium (about 0·23 g.) was dissolved in the medium; *tert.*-butyl chloride (about 1 c.c.) was then added, and the whole made up to 100 c.c. Portions of 5 c.c. were separately sealed up in bulbs, which were placed in the thermostat at 25·0°. Initial estimations of alkali and olefin were carried out as soon as the reaction mixture had been made up. Alkalinity values were found by breaking the bulbs in 100 c.c. of absolute ethyl alcohol and titrating with 0·0495N-acid, lacmoid being used as indicator. The loss of alkalinity during reaction measures the decrease in concentration of *tert.*-butyl chloride between the initial and the final measurements. Olefin was estimated by a standardised bromometric method as follows. The bulbs were cooled by shaking for 1 min. in a carbon dioxide–alcohol freezing mixture, dried externally, and then broken under a mixture of chloroform (70 c.c.), 0·0495N-acid (15 c.c.)

and ice-water (20 c.c.). The whole having been shaken, the chloroform layer was run off, washed with ice-water (50 c.c.), and dried for 5 mins. with calcium chloride. A solution (10 c.c.) of bromine in chloroform, saturated with hydrogen bromide, and standardised immediately before and after use, was then added and allowed to interact with the olefin for 5 mins. Then the unconsumed bromine was estimated as usual by titration with 0·0189N-thiosulphate after addition of potassium iodide and water. Corresponding to the initial and the final alkali determinations, three initial and three final estimations of olefin were carried out for each solvent. The initial olefin values measure the small amount of *iso*butylene produced during the making up of the solutions together with any trace of unsaturated material that may have been present in the reagents. There is no error due to the volatility of *isobutylene*: a full investigation of this method by Mr. S. Masterman has shown that it gives reliable results even with propylene. Thus the difference between the initial and final olefin values represents *iso*butylene formed during the measured disappearance of *tert*.-butyl chloride.

The results are exemplified below for "85%-MeOH," and are summarised for the two media in Table III.

Estimations of alkali (in terms of the volume of 0·0495N-acid equivalent to 5 c.c. of reaction mixture): Initial, 9·72 c.c. Final, 1·12 c.c. Loss, 8·60 c.c.

Estimations of olefin (in terms of the volume of 0·0189N-thiosulphate equivalent to 10 c.c. of the solution of bromine in chloroform, this being the quantity used in association with 5 c.c. of reaction mixture):

(1) Initial: (*A*) Standardisation of bromine solution: Before the estimation, 9·59 c.c. After the estimation, 9·42 c.c. Mean, 9·50 c.c. (*B*) Measurement of residual bromine after reaction with olefin: 8·40, 8·28, 8·07 c.c. Mean, 8·24 c.c. (*C*) Bromine uptake: 9·50 − 8·24 = 1·26 c.c.

(2) Final: (*A*) Mean, 8·60 c.c. (*B*) Mean, 1·25 c.c. (*C*) 7·35 c.c. Therefore olefin formed = (2*C*) − (1*C*) = 7·35 − 1·26 = 6·09 c.c.

TABLE III.

*Estimations of* iso*Butylene.*

(Consumption of $Bu^{\gamma}Cl$ in c.c. of 0·0495N-acid, and formation of $C_4H_8$ in c.c. of 0·0189N-thiosulphate, each equivalent to 5 c.c. of reaction solution.)

| Medium. | Consumption of $Bu^{\gamma}Cl$. | Formation of $C_4H_8$. | Yield of $C_4H_8$ (mols. %). |
|---|---|---|---|
| 70%-MeOH ............ | 8·25 | 4·0 | 9 |
| 85%- „ ............ | 8·60 | 6·1 | 13 |

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## 172. *The Nitration of Benzenesulphonyl Chloride and Fluoride.*

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A modification of the Holleman extraction method for proximate analysis has been elaborated, use being made of the refractive index as a measure of concentration. This has been used to examine the products of the nitration of benzenesulphonyl chloride. The mixed nitrobenzenesulphonyl chlorides were converted into sulphonanilides for analysis by the thermal method and by the modified extraction method. The mixture obtained by nitrating benzenesulphonyl fluoride was examined directly by the thermal method. In the nitration of benzenesulphonyl chloride a trinitrohydroxy-by-product has been detected and shown to amount to 2% of the products.

In a comparison of the $SO_2Cl$ and the $SO_2F$ group with related *m*-directing radicals the results are shown to be in agreement with current views, but one discrepancy which emerges may require further investigation.

THE directive powers of groups $SO_2X$, where X is OH, Cl, O·$CH_3$, and $NR_2$, have been compared in the benzyl series, $C_6H_5·CH_2·SO_2X$ (Ingold, Ingold, and Shaw, J., 1927, 813).

In the simple phenyl series, $C_6H_5{\cdot}SO_2X$, the sulphonic acid is the only substance which has been studied (Obermiller, *J. pr. Chem.*, 1914, **89**, 70). Arising from a comparison recently made between the nitration of substituted sulphonic acids and their chlorides (Turner and Wynne, J., 1936, 707), the nitration of unsubstituted benzenesulphonyl chloride was studied in detail. In order to facilitate the proximate analysis, the easily-hydrolysed nitrated sulphonyl chlorides were converted into the more stable mixed nitrobenzenesulphonanilides. There was obtained a 96% yield of anilides which gave correct ultimate analysis figures. A check experiment showed that the 4% loss was evenly distributed over all three possible products. The mixture was analysed by a thermal method, using the thaw-point device, and by an extraction method (Holleman, " Die Direkte Einführung von Substituenten in den Benzolkern," p. 17) in which the refractive index of the solution was used as a measure of concentration. A suitable extracting liquid of low volatility, low refractive index, and sufficient solvent power was found in amyl valerate.

The first figures obtained by the extraction method were evidently erroneous: their sum was 109·4%, and the proportion of *m*-isomeride (97·9%) greatly exceeded the proportion detected by the thermal method (91·7%). At the same time, artificial mixtures of the three nitrobenzenesulphonanilides could be analysed with the accuracy expected Although special experiments showed that neither under- nor over-nitration had occurred, direct refractive index tests clearly indicated the presence of a fourth substance, formed by some unexplained reaction. Any such substance would be extracted independently and would therefore raise the percentage found in the determination of each isomeride. Moreover, even if the satisfactory ultimate analyses given by the nitration mixture appeared to rule out the presence of an impurity, they would admit a small proportion of a substance not very different in ultimate composition from the anilides.

Direct experiments on the nitration mixture at last successfully separated a specimen of this fourth substance, which was identified as 2 : 4 : 6-trinitro-3-hydroxydiphenylamine (Blanksma, *Rec. Trav. chim.*, 1902, **21**, 261; Ullmann and Bruck, *Ber.*, 1908, **41**, 3939). A direct extraction test proved the absence of any fifth substance.

The presence of this diphenylamine implied that during the nitration some trinitro-*m*-hydroxybenzenesulphonyl chloride had been formed as a by-product. When this subsequently reacted with aniline, the entire sulphonyl chloride group was eliminated. The occurrence of hydroxy-by-products in the nitration of benzene, toluene, and xylene was noted many years ago (Nölting, *Ber.*, 1885, **18**, 2670; 1888, **21**, 3158) and emphasised by Armstrong and Rossiter (P., 1891, **7**, 89). It appears to have been investigated no further except for nitrations in the presence of mercuric salts. The formation of such by-products in other simple nitrations will be discussed in a future paper.

Theoretically the Holleman extraction method may be applied to a mixture containing any number of components, although hitherto its use appears to have been confined to mixtures of not more than three. To analyse a four-component mixture, four concentration–refractive index curves are required: these were therefore constructed. The proportions determined were: *o*-, 5·8; *m*-, 91·6; *p*-, 2·4; trinitrodiphenylamine, 2·0% (total 101·8%). These figures were reduced to a 100% basis, and corrected for differences in molecular weight: the products of nitration are then given as: *m*-, 91·3 ± 0·5; *o*-, 5·2 ± 1; *p*-, 1·8 ± 1; by-product, 1·7 ± 1%.

It was impossible to convert the nitrobenzenesulphonyl fluorides quantitatively into anilides; the proximate analysis here was therefore carried out directly by the thermal method. The proportion of *m*-product was 95·6 ± 0·5%.

These figures (sulphonic chloride, 91·3% *m*-; fluoride, 95·6% *m*-) are to be compared with those obtained by Obermiller in the nitration of the sulphonic acid (63% *m*-, 27% *o*-, 10% *p*-). The contrast between the nitration of an acid and its chloride is well known and easily explained (compare Bennett, J., 1936, 715). The observed difference between sulphonyl fluoride and chloride would also have been anticipated.

Comparison of the inductive effects of methyl and chlorine would seem to indicate the sulphonic chloride group as more powerfully *m*-directing than the methanesulphonyl group. This conclusion was justified in the benzyl series (Ingold, Ingold, and Shaw, *loc. cit.*), where benzylmethylsulphone yields 30% of *m*-nitration product and benzylsulphonyl chloride

51%. Yet the figure of 91·3% for benzenesulphonyl chloride must be contrasted with one of 97—98% for phenylmethylsulphone (Twist and Smiles, J., 1925, **127**, 1278; Baldwin and Robinson, J., 1932, 1445). It is possible that the higher *m*-directing power of the sulphone may be explained by its superior tendency to unite with the sulphuric acid present, a tendency which increases the proportion of *m*-isomeride in nitration and has already been demonstrated for benzaldehyde (Baker and Moffitt, J., 1931, 314); but the figure quoted by Twist and Smiles was admittedly not a precise estimate, and those quoted by Baldwin and Robinson represent more a comparison of related substances than an absolute value for any one. The question might be settled by a more detailed investigation of the nitration of phenylmethylsulphone.

## Experimental.

### I. *Nitration of Benzenesulphonyl Chloride.*

*Preparation of the Three Nitrobenzenesulphonanilides.*—For accurate analyses, the anilides described below were recrystallised three times from alcohol and once from benzene. (a) *m*-Nitrobenzeuesulphonanilide, m. p. 125°. (b) *o*-Nitrobenzenesulphonanilide, m. p. 115°, was made by oxidising *oo'*-dinitrodiphenyl disulphide to *o*-nitrobenzenesulphonic acid (Blanksma, *Rec. Trav. chim.*, 1901, **20**, 115), converting the powdered anhydrous acid into its chloride (Ullmann, *Ber.*, 1910, **43**, 2700), and treating the chloride with aniline. Low yields of sulphonyl chloride may possibly be explained by the formation and breakdown of a sulphinyl chloride (compare Turner and Wynne, J., 1936, 701).

(c) p-*Nitrobenzenesulphonanilide.* *pp'*-Dinitrodiphenyl disulphide, prepared from sodium disulphide and *p*-chloronitrobenzene (Blanksma, *loc. cit.*), melted at 181° after repeated crystallisation from benzene, acetic acid, and ethyl acetate. This substance has been described as melting at 171° (Blanksma, *loc. cit.*; Elgersma, *Rec. Trav. chim.*, 1929, **48**, 752; Zincke, *Annalen*, 1913, **400**, 1), and the existence of two forms has been asserted (Hodgson and Wilson, J., 1925, **127**, 440). All these observations are explained by the presence in the crude disulphide of quantities of the monosulphide. Our crude material melted from 145° to 180°, and in the tedious purification we isolated a specimen of the monosulphide, m. p. 153—157°, identical with a specimen prepared by condensing potassium *p*-nitrothiophenoxide with *p*-bromonitrobenzene in alcohol. Oxidised with fuming nitric acid, both specimens yielded the sulphoxide, m. p. 177—179° (Found: C, 49·7; H, 2·5; N, 9·5; S, 10·9. Calc.: C, 49·4; H, 2·7; N, 9·6; S, 10·9%), and, with chromic acid mixture, the sulphone, m. p. 251—254° (Found: S, 10·5. Calc.: S, 10·4%). Fromm and Wittmann (*Ber.*, 1908, **41**, 2269) gave this m. p. as 282°.

The disulphide was oxidised to the sulphonic acid by means of fuming nitric acid. When the crude disulphide was used, *pp'*-dinitrodiphenyl sulphoxide (m. p. 179°, mentioned above) was formed as a by-product insoluble in water (cf. Witte, *Rec. Trav. chim.*, 1932, **51**, 290). The acid chloride from the potassium salt yielded p-*nitrobenzenesulphonanilide*, m. p. 171° (Found: C, 51·7; H, 3·3. $C_{12}H_{10}O_4N_2S$ requires C, 51·8; H, 3·6%).

*Crystal Forms of the Above Anilides.*—(i) m-*Nitrobenzenesulphonanilide.* This substance crystallises in the sphenoidal class of the monoclinic system, the development being clearly enantiomorphous; both left- and right-handed crystals were observed. The elements are $a:b:c = 1·938:1:1·651$; $\beta = 118° 0'$.

The forms observed were *a*(100), *r*(101), *c*(001), *R*($\bar{1}$01), *m*(110), *m'*(1$\bar{1}$0), and either *q*(011) or *q'*(0$\bar{1}$1). The typical habit of a right-handed crystal from alcohol is shown in Fig. 2. The following angular values were obtained from six crystals, from measurements on the two-circle goniometer :—

| | *a*(100). | *m*(110). | *r*(101). | *c*(001). | *R*($\bar{1}$01). | *q*(011). |
|---|---|---|---|---|---|---|
| $\phi$ .................... | 0° 0′ | *59° 42′ | 0° 0′ | 0° 0′ | 180° 0′ | *72° 10′ |
| $\rho$ .................... | 90° 0′ | 90° 0′ | 56° 47′ | *28° 0′ | 23° 4′ | *60° 2′ |

The following are the Barker classification angles: *cr* (001 : 101) = 28° 47′; *ra*(101 : 100) = 33° 13′; *am*(100 : 110) = 59° 42′; *bq*(010 : 011) = 34° 37′.

A straight extinction was observed on *a*. The substance has a high double refraction and dispersion. In convergent light, an optic axis is visible emerging perpendicular to the face *c*, and from the appearance of the brushes it is clear that the optic axial angle is near 90°.

(ii) o-*Nitrobenzenesulphonanilide.* The substance crystallises in the monoclinic system with axial ratios $a:b:c = 1·650:1:0·938$, and axial angle $\beta = 118° 59'$. The following is a list of the forms observed and the mean angular measurements obtained from two selected crystals:

| | *a*(100). | *l*(210). | *m*(110). | *r*(101). | *R*(I01). | *o*(111). | *q*(011). | *p*(I11). |
|---|---|---|---|---|---|---|---|---|
| $\phi$ ............ | 0° 0′ | 35° 54′ | *55° 17′ | 0° 0′ | 180° 0′ | 37° 55′ | *59° 27′ | 95° 31′ |
| $\rho$ ............ | 90° 0′ | 90° 0′ | 90° 0′ | 50° 15′ | 5° 10′ | 56° 44′ | *47° 27′ | 43° 15′ |

The usual habit is shown in Fig. 1, with *R* large. The Barker classification angles (observed or calculated) are: *cr*(001 : 101) = 21° 16′; *ra*(101 : 100) = 39° 45′; *am*(100 : 110) = 55° 17′; *bq*(010 : 011) = 50° 38′.

FIG. 1.

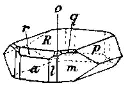



FIG. 2.

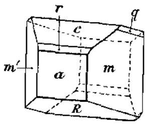
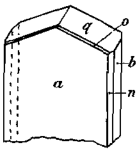



FIG. 3.




A straight extinction, observed on the face *R*, confirmed the position of the plane of symmetry. The optic axes were not observed.

(iii) p-*Nitrobenzenesulphonanilide*. The crystals from various solvents were imperfect and formed curved faces: the measurements are less accurate than those for the other two isomerides. Examination of five crystals gave the following angles:

| | *a*(100). | *n*(120). | *b*(010). | *o*(111). | *q*(011). |
|---|---|---|---|---|---|
| $\phi$ ........................ | 0° 0′ | 70° 50′ | 90° 0′ | *32° 43′ | *49° 6′ |
| $\rho$ ........................ | 90° 0′ | 90° 0′ | 90° 0′ | *36° 57′ | *28° 10′ |

The habit of these crystals is illustrated in Fig. 3. The substance is monoclinic, with axial angle $\beta$ = 109° 19′ and axial ratios $a : b : c$ = 1·443 : 1 : 0·405. The Barker classification angles are: *cr*(001 : 101) = 13° 1′; *ra*(101 : 100) = 57° 40′; *am*(100 : 110) = 53° 43′; *bq*(010 : 011) = 69° 6′.

The straight extinction on the face *a* confirms the position of the plane of symmetry.

*Sodium Salts of the Nitrobenzenesulphonanilides.*—From concentrated sodium hydroxide solutions the sodium salts of the anilides crystallised out; their considerable solubility in water prevented adequate washing of the crystals. The sodium content of the salts was found by direct titration against 0·1N-hydrochloric acid, results being consistently 0·6% high because of adsorbed alkali. The *sodium* salt of *m*-nitrobenzenesulphonanilide (Found: Na, 7·4. $C_{12}H_9O_4N_2SNa,2H_2O$ requires Na, 6·9%) when heated afforded the red anhydrous salt (Found: loss, 11·2. $2H_2O$ requires loss, 10·8%. Found, in anhydrous salt: Na, 8·5. $C_{12}H_9O_4N_2SNa$ requires Na, 7·7%). The yellow dihydrated salt of *o*-nitrobenzenesulphonanilide (Found: Na, 7·45%) when heated lost $2H_2O$ (Found: loss, 12·6%), partly liquefied, and cooled to give a red anhydrous solid (Found: Na, 8·5%). *p*-Nitrobenzenesulphonanilide gave only an anhydrous vermilion salt (Found: Na, 8·3%).

*Thermal Examination of the System*: o-, m-, p-*Nitrobenzenesulphonanilides.*—Observations were made by the thaw-point method (Rheinboldt and Kircheisen, *J. pr. Chem.*, 1926, **113**, 348; cf. Bennett and Wain, J., 1936, 1118): the temperatures are corrected, $T_1$ being the point at which liquid was first detected and $T_2$ that at which the last solid disappeared. The mixed molten anilides set to a glass unless incubated 10° below their eutectic temperature.

(i) *System* m- *and* o-*nitrobenzenesulphonanilide.*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *o*-Anilide, mols. % ............ | 0·0 | 3·7 | 9·1 | 9·2 | 11·4 | 14·2 | 17·1 |
| $T_2$ .................................. | 124·8° | 121·6° | 119·0° | 119·6° | 117·6° | 116·1° | 115·3° |
| *o*-Anilide, mols. % ............ | 19·3 | 21·2 | 44·2 | 70·9 | 100·0 | | |
| $T_2$ .................................. | 112·7° | 112·2° | 101·1° | 101·7° | 115·4° | | |
| *o*-Anilide, mols. % ............ | 29·8 | 50·9 | 51·8 | 61·7 | 76·9 | 80·0 | 89·7 |
| $T_2$ .................................. | 109·7° | 96·3° | 92·2° | 96·5° | 104·9° | 110·6° | 112·4° |
| $T_1$ .................................. | 88·7 | 87·9 | 87·4 | 87·5 | 88·2 | 87·8 | 89·0 |

The curve shows a simple eutectic at 87·7°, 55 mols. % of *o*-nitrobenzenesulphonanilide.

(ii) *System* m- *and* p-*nitrobenzenesulphonanilide.*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| $p$-Anilide, mols. % | 0·0 | * 2·8 | 3·2 | 6·8 | 9·5 | 13·8 | 16·4 |
| $T_1$ | — | 109·1° | 108·3° | 108·3° | 108·3° | 108·1° | 108·8° |
| $T_2$ | 124·2 | 122·5 | 122·2 | 120·8 | 118·8 | 117·1 | 115·2 |
| $p$-Anilide, mols. % | 18·7 | 21·8 | 22·5 | 24·8 | 28·8 | 31·2 | 38·2 |
| $T_1$ | 107·9° | 107·9° | 108·2° | 107·8° | 108·6° | 108·3° | 108·3° |
| $T_2$ | 113·8 | 112·2 | 111·9 | 112·0 | 114·8 | 118·5 | 125·5 |
| $p$-Anilide, mols. % | 41·6 | 51·3 | 61·2 | 66·1 | 78·0 | 85·0 | 100·0 |
| $T_1$ | 108·0° | 109·2° | 108° | 107° | 108° | 110° | — |
| $T_2$ | 129·9 | 139·2 | 150 | 152 | 160 | 165 | 171° |

The curve shows a simple eutectic at 108·3°, 24 mols. % of *p*-nitrobenzenesulphonanilide.

(iii) *System* o- *and* p-*nitrobenzenesulphonanilide.*

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| $p$-Anilide, mols. % | 10·4 | 19·1 | 30·2 | 40·8 | 59·4 | 59·8 | 70·6 | 77·8 | 89·1 |
| $T_1$ | 103·4° | 103·8° | 103·8° | — | 104·0° | — | — | — | — |
| $T_2$ | 110·9 | 105·7 | 120·1 | 131·9° | — | 147·1° | 156° | 160½° | 166½° |

The curve shows a simple eutectic at 103·8°, 18 mols % of *p*-nitrobenzenesulphonanilide.

(iv) *The ternary eutectic.* The mean value of the ternary eutectic temperature was 82·2°, determined by the thaw-point method; no eutectic temperatures could be detected on cooling curves.

*Nitration of Benzenesulphonyl Chloride.*—During 1 hour, a weighed amount (about 6 g.) of benzenesulphonyl chloride (m. p. 15·5°) was dropped slowly into a stirred mixture of nitric acid (5 c.c., 100%) and sulphuric acid (20 c.c., 100%) held at 30°. The product was not affected by severer precautions against overheating, by altering the time of nitration from 15 to 140 minutes, by twice redistilling the benzenesulphonyl chloride, or by using more nitric (25 c.c.) and less sulphuric acid (5 c.c.) at 60°. The nitration mixture was poured on ice, and the precipitated chlorides extracted with benzene. Their solution was dried by the addition of thionyl chloride (3 c.c.), driven off by an hour's boiling. A further hour's heating with aniline (20 c.c., redistilled) gave the sulphonanilides, which were extracted by warm 2N-sodium hydroxide, and precipitated by an excess of dilute nitric acid (1 : 1). Yields averaged 96%. Pure *m*-nitrobenzenesulphonanilide was obtained in 99% yield from *m*-nitrobenzenesulphonyl chloride by this method. Each of the three anilides could be recovered pure and without appreciable loss from the benzene solution by this extraction method.

The mixed anilides without further purification gave no reactions for sodium ion, chloride, or aniline, and analysed correctly (Found, for one individual nitration product: C, 51·7; H, 3·5; S, 11·3; N, 9·9; for the mixed products of six nitrations: * C, 51·6; H, 3·7; S, 11·3; N, 10·1. Calc.: C, 51·8; H, 3·6; N, 10·1; S, 11·5%).

*Analysis of the Nitration Product* (*Series A*).—(i) *By direct fractional crystallisation.* From benzene, 80% was obtained as *m*-nitrobenzenesulphonanilide.

(ii) *Thermal analysis.* Both *o*- and *p*-nitrobenzenesulphonanilide depressed the m. p. of the *m*-isomer to approximately equivalent extents (cf. Nichols, *J. Amer. Chem. Soc.*, 1918, **40**, 400). The extent of this depression was determined by the thaw-point method :

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| $o$-Anilide, mols. % | 3·7 | 9·1 | 9·2 | 11·4 | 14·2 | 17·1 | 19·3 | 21·2 | 29·8 |
| $T_2$ | 121·6° | 119·0° | 119·6° | 117·5° | 116·1° | 115·3° | 112·7° | 112·2° | 109·7° |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $p$-Anilide, mols. % | 2·8 | 3·2 | 6·8 | 9·5 | 13·8 | 16·4 | 18·7 | 21·8 | 22·9 | 24·8 | 28·8 |
| $T_2$ | 122·5° | 122·2° | 120·8° | 118·8° | 117·1° | 115·2° | 113·8° | 112·2° | 111·9° | 112·0° | 114·8° |

An artificial mixture was analysed from the value of $T_2$ determined by the thaw-point method (Found : *m*-, 89·3. Mixture contained : *m*-, 90·0 ; *o*-, 6·0 ; *p*-, 4·0%). To check the thaw-point figures, cooling curves were plotted, by cooling about 10 g. of the mixture in a bath whose temperature was held 4° below that of the mixture. The curves obtained showed a bowl-shaped portion due to supercooling, followed by a peak and a final straight line; $T_2$ was obtained by extrapolating back from the straight portion to the original downward slope. No eutectic could be detected by careful cooling (Found, by cooling curves, *m*-, 90·4%).

For clearer vision with the dark-coloured nitration mixture, thaw-point tubes with an oval cross-section were used; $T_2$ was determined as 119·43°, and from cooling curves as 119·45°. The nitration mixture therefore contains 91·7% of *m*-nitrobenzenesulphonanilide.

(iii) *Extraction method.* The refractive index, determined on an Abbé refractometer, was

* Analyses by Weiler: unmarked analyses by Schoeller.

chosen as a measure of solubility. Amyl valerate (b. p., 190°; $n_D^{20°}$, 1·4130) was chosen as solvent because its high b. p. minimised evaporation, because it dissolved about 5% each of the anilides, and because, its refractive index being low, a small amount of dissolved highly-refractive anilide would be easily detected. Suitable amounts of amyl valerate and the anilides were stirred in tubes in a thermostat (20° ± 0·1°) for 3 hours, and were allowed to recover for an hour from the heat generated by stirring.

The solubility of the third anilide in a solution saturated with the other two was measured by the increasing refractive index. Curves were drawn and checked against a made-up mixture. The nitration mixture was analysed from these curves to contain nitrobenzenesulphonanilides : *o*-, 6·9; *m*-, 97·9; *p*-, 4·6% (total 109·4%). Repetitions of the nitration and the analysis under various conditions made it clear that this figure was in excess of 100% not as a result of any impurity in the materials or of under- or over-nitration. After many experiments it was concluded that the 9·4% excess must be due to the presence in the nitration mixture of a fourth substance. A direct test was possible : the refractive index of a solution saturated with the three anilides was 1·4310, and after this solution had been stirred with an amount of nitration product corresponding to 23 g. per 100 g. of amyl valerate the value was 1·4324, the increase of 0·0014 indicating a fourth substance.

*A Hydroxy-by-product.*—When the nitration mixture was stirred with water, part dissolved to a slightly acid, yellow solution, from which mineral acids precipitated a yellow solid (X). To isolate this substance in quantity, 1250 g. of benzenesulphonyl chloride were nitrated and converted into mixed sulphonanilides, which were extracted with hot 2% sodium acetate solution. The cold filtered extracts were acidified, and the yellow solid collected and purified. It formed yellow needles, m. p. 161—162°, from acetic acid. The substance was identified as 2 : 4 : 6-trinitro-3-hydroxydiphenylamine (Found : C, 45·2; H, 2·7; N, 16·9. Calc. : C, 45·0; H, 2·5; N, 17·5%), identical with that synthesised from *m*-nitrophenol (Blanksma, *Rec. Trav. chim.*, 1902, **21**, 261) and from styphnic acid (Ullmann and Bruck, *Ber.*, 1908, **41**, 3939). Both X and the synthetic material with *p*-toluenesulphonyl chloride and diethylaniline gave small orange prisms of 3-*chloro*-2 : 4 : 6-*trinitrodiphenylamine*, m. p. 147—148° (Found : C, 43·0; H, 2·2; N, 16·8; Cl, 10·7. $C_{12}H_7O_6N_4Cl$ requires C, 42·5; H, 2·7; N, 16·5; Cl, 10·5%), which condensed with aniline to give 2 : 4 : 6-trinitro-1 : 3-dianilinobenzene, m. p. 215—216° (compare 207°; Van Duin, *Rec. Trav. chim.*, 1919, **38**, 93) (Found : N, 17·95. Calc.: N, 17·7%), and with piperidine to afford the *piperidino*-compound, yellow plates with a straight extinction, m. p. 161—162° (Found : C, 52·7; H, 4·4; N, 18·1. $C_{17}H_{17}O_6N_5$ rquires C, 52·6; H, 4·4; N, 18·0%).

*Analysis of the Nitration Product* (*Series B*).—(i) *The extraction method.* Four refractive-index curves were obtained : the symbols $W_o$, $W_m$, $W_p$, $W_X$ denote respectively the weights of *o*-, *m*-, *p*-nitrobenzenesulphonanilides and 2 : 4 : 6-trinitro-3-hydroxydiphenylamine per 100 g. of amyl valerate. About 1 c.c. of solution was sufficient for one determination. The figures for the curves were :

(*a*) Amyl valerate saturated with *o*-, *p*-, and X; increasing amounts of *m*- added.

| | | | | | |
|---|---|---|---|---|---|
| $W_m$ | 0·00 | 2·03 | 3·29 | 5·53 | 7·75 |
| $n$ | 1·42325 | 1·4260 | 1·4280 | 1·4310 | 1·4346 |

(*b*) Saturated with *m*-, *p*-, and X; increasing amounts of *o*-.

| | | | | | | |
|---|---|---|---|---|---|---|
| $W_o$ | 0·00 | 0·48 | 0·59 | 1·185 | 1·82 | 3·76 |
| $n$ | 1·4291 | 1·4299 | 1·4300 | 1·4310 | 1·4315 | 1·4344 |

(*c*) Saturated with *o*-, *m*-, and X; increasing amounts of *p*-.

| | | | | | | |
|---|---|---|---|---|---|---|
| $W_p$ | 0·00 | 0·445 | 0·70 | 0·78 | 0·96 | 1·56 |
| $n$ | 1·4326 | 1·4333 | 1·43345 | 1·4338 | 1·4340 | 1·43505 |

(*d*) Saturated with *o*-, *m*-, and *p*-; increasing amounts of X.

| | | | | |
|---|---|---|---|---|
| $W_X$ | 0·00 | 0·475 | 1·12 | 1·57 |
| $n$ | 1·4310 | 1·4318 | 1·4332 | 1·4343 |

A new nitration mixture was prepared, the final precipitation of the anilides being carried out slowly at 0°, with vigorous stirring to minimise ultimate sampling errors (Found : C, 51·8; H, 3·2; S, 11·1; N, 10·2%). The refractive index of a solution saturated with all four components was approached by long stirring, and by cooling a solution saturated at 50° : $n$ = 1·4360. When this solution was stirred with an amount of the new nitration mixture corresponding to 23 g. per

100 g. of solvent, the refractive index was unchanged. Therefore no fifth substance was present. From the curves, the nitration mixture was analysed to : *o*-, 5·8 ; *m*-, 91·6 ; *p*-, 2·4 ; X, 2·0%.

| Component. | *o*-. | *o*-. | *m*-. | *m*-. | *p*-. | *p*-. | X. | X. |
|---|---|---|---|---|---|---|---|---|
| Wt. of mixture ...... | 0·1029 | 0·1007 | 0·0518 | 0·0513 | 0·1000 | 0·0977 | 0·0995 | 0·1011 |
| Wt. of solvent ...... | 1·0192 | 1·1416 | 1·1697 | 1·0519 | 1·0254 | 1·0874 | 1·0399 | 1·0774 |
| $n$ ...................... | 1·4300 | 1·42985 | 1·42905 | 1·4297 | 1·42205 | 1·4329 | 1·4314 | 1·43135 |
| $W$ ...................... | 0·61 | 0·52 | 4·04 | 4·50 | 0·28 | 0·18 | 0·20 | 0·18 |
| % ...................... | 6·04 | 5·49 | 91·0 | 92·2 | 2·87 | 2·00 | 2·09 | 1·91 |

The probable error of the *m*-determination is of the order ± 0·5% ; of the others, ± 1·0%.

As a further check on the trustworthiness of the whole process, 6 g. of a mixture of *o*- (6·0%), *m*- (90·0%), and *p*- (4·0%) nitrobenzenesulphonyl chlorides were stirred with nitric acid (5 c.c., 100%) and sulphuric acid (20 c.c., 100%). The product was isolated as a 96% yield of mixed nitrobenzenesulphonanilides, of unchanged composition : *m*-, 91·8 (thermal analysis) ; *m*-, 90·3 ; *o*-, 6·8 ; *p*-, 5·9% (extraction method). The *p*-determination is the least accurate owing to the low solubility of the *p*-anilide.

(ii) *Thermal analysis.* To the figure previously determined, a correction must be made for the difference in molecular weight of *m*-nitrobenzenesulphonanilide (278) and 2 : 4 : 6-trinitro-3-hydroxydiphenylamine (320) ; the final figure becomes 91·45%, which a consideration of probable errors shows as accurate to ± 0·5%.

*Summary.*—Reducing these figures to a 100% basis, and allowing for the formation of the diphenylamine by a chemical reaction different from anilide formation, we find that in the nitration of benzenesulphonyl chloride, there are formed 91·3 ± 0·5, 5·2 ± 1, and 1·8 ± 1%, respectively, of *m*-, *o*-, and *p*-nitrobenzenesulphonanilide and 1·7 ± 1% of 2 : 4 : 6-trinitro-3-hydroxybenzenesulphonyl chloride.

## II. *Nitration of Benzenesulphonyl Fluoride.*

Benzenesulphonyl fluoride, prepared by the method of Davies and Dick (J., 1931, 2104), was redistilled to constant b. p. (93°/14·5 mm.) (Found : equiv. by hydrolysis, 79·8. Calc. : 80·0).

The isomeric nitrobenzenesulphonyl fluorides were obtained by similar methods : *m*-nitrobenzenesulphonyl fluoride, m. p. 45—46° [Found : equiv. by hydrolysis after 4 hours' boiling with 0·5N-sodium hydroxide, 102·5. Calc. : 102·5. (A blank titration was necessary because of the solvent action of the alkali on the flask)] ; p-*nitrobenzenesulphonyl fluoride*, m. p. 79° (Found : C, 35·4 ; H, 2·0 ; N, 7·1 ; equiv. by hydrolysis, 102·5. $C_6H_4O_4NSF$ requires C, 35·1 ; H, 2·0 ; N, 6·8%) ; o-*nitrobenzenesulphonyl fluoride*, m. p. 59° (Found : C, 35·6 ; H, 2·1 ; N, 7·0% ; equiv., 102·5).

*Nitration.*—Benzenesulphonyl fluoride was nitrated with a mixture of nitric acid (15 c.c., 100%) and sulphuric acid (25 c.c., 100%). As it was found impossible to convert *m*-nitrobenzenesulphonyl fluoride quantitatively into its anilide, the product here was extracted with chloroform, subsequently removed by prolonged evaporation. Yield, 97% (equiv., 102·5) ; the nitration mixture hydrolysed to an orange solution.

The depression of the m. p. of *m*-nitrobenzenesulphonyl fluoride by the *p*-isomeride was determined :

| | | | | | |
|---|---|---|---|---|---|
| *p*-Fluoride, mols. % .................... | 0·0 | 0·99 | 2·10 | 4·04 | 7·35 |
| $T_2$ .............................................. | 45·6° | 45·5° | 44·65° | 43·8° | 42·45° |

Determinations of $T_2$ on the nitration mixture gave 43·63° by the thaw-point method, and 43·65° by a cooling curve, corresponding to 95·6% of *m*-fluoride.

When, by the addition of *p*-fluoride to the nitration mixture, the percentage of *m*- was reduced to 91·0%, $T_2$ determinations (41·5°) detected 91·2% *m*-fluoride.

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The University, Sheffield. [*Received, March* 31*st*, 1938.]

# 173. *The Introduction of the* MgBr *Group into Anisole and Phenetole.*

By Frederick Challenger and Samuel A. Miller.

In the hope of preparing di-2-thienyl disulphide and thence thiophen-2-thiol, 2-thienylmagnesium bromide was heated with sulphur in presence of phenetole as a high-boiling solvent. The desired product was not obtained, but a thiol was finally isolated which, with chloroacetic acid, gave a compound having the composition $EtO·C_6H_4·S·CH_2·CO_2H$. The MgBr group having apparently entered the phenetole nucleus with elimination of thiophen, the course of the reaction was studied.

When phenetole was boiled with ethylmagnesium bromide and then treated with ether and mercuric bromide, *o*-phenetylmercury bromide, $EtO·C_6H_4·HgBr$, was obtained, and converted into di-*o*-phenetylmercury, $Hg(C_6H_4·OEt)_2$. Similarly, anisole with ethylmagnesium bromide or *n*-propylmagnesium bromide gave *o*-anisylmercury bromide, characterised as the corresponding iodide and chloride, and as di-*o*-anisylmercury. No *p*-compounds were isolated. Phenetole does not react appreciably with sulphur at its boiling point, nor is anisole or phenetole mercurated by boiling ethereal mercuric chloride or bromide. Interaction of ethylmagnesium bromide and boiling dimethylaniline, followed by treatment with carbon dioxide, gave dimethylanthranilic acid. *p*-Dimethylaminobenzoic acid, obtained by other workers under more drastic conditions, was not detected. The formation of *o*-derivatives in these experiments is possibly facilitated by formation of co-ordination compounds between the Grignard reagent and the phenol ether or dimethylaniline.

For the purposes of another investigation it was proposed to synthesise 2-thienylthiolacetic acid, $C_4H_3S·S·CH_2·CO_2H$, from thiophen-2-thiol (Biedermann, *Ber.*, 1886, **19**, 1616), chloroacetic acid, and sodium hydroxide. Phenylthiolacetic acid is readily prepared by the analogous method (Ramberg, *Z. physikal. Chem.*, 1900, **34**, 562).

Biedermann obtained only 0·5 g. of the thiol from 30 g. of thiophen-2-sulphonyl chloride and V. Meyer also isolated only small quantities as a by-product during the large-scale synthesis of thiophen from sodium succinate and phosphorus trisulphide (*Ber.*, 1887, **20**, 1756). A more promising method appeared to be that of Taboury (*Bull. Soc. chim.*, 1903, **29**, 761), who found that sulphur reacts with phenyl- and α-naphthyl-magnesium bromides at 0°, giving on acidification the corresponding thiols and disulphides. One of us and Harrison (*J. Inst. Pet. Tech.*, 1935, **21**, 153) obtained di-2-thienyl sulphide, $(C_4H_3S)_2S$, from sulphur and 2-thienylmagnesium bromide, but were unable to obtain a thiol or disulphide.

The present authors modified this procedure by carrying out the reaction in boiling phenetole, but could not obtain a homogeneous product, much polysulphide being produced. The mixture on reduction yielded a thiol; this with chloroacetic acid gave a product which was not a thiophen derivative but a *phenetylthiolacetic acid*, $EtO·C_6H_4·S·CH_2·CO_2H$. This was not due to formation of a phenetylthiol by direct union of the phenetole with sulphur, since this can be almost quantitatively recovered from boiling phenetole. The MgBr group would therefore appear to have entered the nucleus, the resulting phenetylmagnesium bromide then reacting with sulphur according to the Taboury reaction:

$$EtO·C_6H_4·H + C_4H_3S·MgBr = EtO·C_6H_4·MgBr + C_4H_4S$$

Confirmation of this view was afforded by addition of mercuric bromide and ether to the product obtained from ethylmagnesium bromide and boiling phenetole; *o*-phenetylmercury bromide, $EtO·C_6H_4·HgBr$ (Michaelis, *Ber.*, 1894, **27**, 261), was readily isolated. This is in accordance with the general behaviour of Grignard reagents to mercuric halides (Hilpert and Grüttner, *Ber.*, 1913, **46**, 1686; 1915, **48**, 906). No other mercury derivative was detected. Potassium iodide in alcohol converted this into di-*o*-phenetylmercury (see p. 895).

The reaction was then extended to anisole, ethylmagnesium bromide being used; after treatment with mercuric bromide as before, the only product was *o*-anisylmercury bromide, m. p. 186—187°. This compound is described by Michaelis (*loc. cit.*, p. 257) as having m. p. 183°. With potassium iodide and alcohol it gave *o*-anisylmercury iodide which with sodium iodide in acetone yielded di-*o*-anisylmercury. (When an alkali iodide reacts with

an arylmercury halide, either an arylmercury iodide, or diarylmercury and sodium mercury iodide are produced : $2RHgX + 2NaI = R_2Hg + HgI_2 + 2NaX$. Compare Steinkopf, *Annalen*, 1917, **413**, 310.) The di-*o*-anisylmercury so obtained was converted by mercuric chloride into *o*-anisylmercury chloride (Whitmore and Middleton, *loc. cit.*).

*o*-Anisylmercury bromide (m. p. 186—187°) was also prepared from *n*-propylmagnesium bromide and boiling anisole, followed by treatment with ethereal mercuric bromide. It was shown in separate experiments that phenetole and anisole are not mercurated by boiling ethereal solutions of mercuric chloride or bromide.

These results indicate that substitution of the MgBr group for a hydrogen atom in anisole or phenetole under the conditions of these experiments occurs exclusively in the *o*-position (see p. 896).

This conclusion has been confirmed in the case of anisole by Dr. E. Rothstein, who has submitted the products from two separate experiments (with ethylmagnesium bromide) to a careful fractional crystallisation. Only *o*-anisylmercury bromide and some ethylmercury bromide could be isolated.

The recorded m. p. of *p*-anisylmercury bromide, 187°, seemed open to suspicion, as *p*-anisylmercury chloride melts at 239° (Michaelis aud Rabinerson, *Ber.*, 1890, **23**, 2344) and an inspection of the m. p.'s of several corresponding organo-mercury chlorides and bromides shows that these lie fairly close together and often differ by less than 10°. Differences of over 50° do not occur.

The point was of importance, since, if *p*-anisylmercury bromide melts at 187°, it might appear that substitution of MgBr in the anisole nucleus had taken place in the *p*-position. In view of the transformations to which the reaction product was submitted (see above), and of the *o*-substitution observed in phenetole, this would seem highly improbable. Nevertheless, a further study was made of the *o*- and *p*-anisylmercury bromides.

*p*-Anisylmagnesium bromide with mercuric chloride and bromide gave *p*-anisylmercury chloride, m. p. 237—238°, and *p*-anisylmercury bromide, m. p. 241—242°, respectively.

Similarly *o*-anisylmagnesium bromide gave *o*-anisylmercury bromide, m. p. 186°, identical in m. p. and mixed m. p. with the product obtained from anisole and ethyl- or *n*-propyl-magnesium bromide. We have also prepared *o*- and *p*-auisylmercury bromides by the method of Nesmejanow (*Ber.*, 1929, **62**, 1010), confirming these results. Michaelis was therefore in error in stating that *p*-anisylmercury bromide melts at 187°. The correct figure is 241—242°.

o- and p-*Anisyldiazoniummercury bromides*, $MeO{\cdot}C_6H_4N_2{\cdot}HgBr_3$ and $(MeO{\cdot}C_6H_4N_2)_2HgBr_4$, have not previously been described.

The fact that boiling phenetole and anisole react with alkylmagnesium halides was first observed by Grignard (*Compt. rend.*, 1910, **151**, 322), who obtained phenol on acidification of the reaction product. Simonis and Remmert (*Ber.*, 1914, **47**, 269), on heating methylmagnesium iodide with anisole, obtained ethane and (on acidification) phenol: $Ph{\cdot}OMe + MgMeI = Ph{\cdot}O{\cdot}MgI + Me{\cdot}Me$. Phenetole similarly gave phenol and a gaseous product, stated to be propane. Späth (*Ber.*, 1914, **47**, 766), however, showed this gas to be a mixture of hydrocarbons. Grignard and Ritz (*Bull. Soc. chim.*, 1936, **3**, 1181) made a comprehensive study of this type of reaction. The gases were always mixtures, phenetole and methylmagnesium iodide giving ethane, ethylene, and propane and with ethylmagnesium iodide, ethane, ethylene, and butane. Magnesium iodide was also found to react with anisole according to the equation $Ph{\cdot}OMe + MgI_2 = Ph{\cdot}O{\cdot}MgI + MeI$.

Similar results are recorded by Späth (*Monatsh.*, 1914, **35**, 319), who also examined benzyl alkyl ethers, *e.g.*, $CH_2Ph{\cdot}OEt + MgMeI = EtO{\cdot}MgI + CH_2Ph{\cdot}Me$. This reaction is analogous to that of the Grignard reagent on acetals (Tschitschibabin, *Ber.*, 1904, **37**, 186).

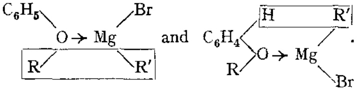
In none of this earlier work is any mention made of the entry of an MgX group into the aromatic nucleus. As the products of reaction were always decomposed by water or dilute acid, any anisyl- or phenetyl-magnesium bromide formed would be reconverted into the phenol ether and so escape detection.

Furthermore, under the conditions of our experiments this reaction occurs to a relatively small extent. With phenetole the yield of organo-mercury bromide was 24%, but with anisole only 3 and 9—11%, calculated on the magnesium, was obtained from *n*-propyl bromide and ethyl bromide respectively.

Interaction with alkylmagnesium bromide has, however, been shown to effect the introduction of MgBr into the methylene group of indene, *cyclo*pentadiene, and fluorene (Grignard and Courtot, *Compt. rend.*, 1911, **152**, 272, 1493; 1914, **158**, 1763; Courtot, *Ann. Chim.*, 1915, **4**, 76) and into the 2-position in thionaphthen (Weissgerber and Krüber, *Ber.*, 1920, **53**, 1557).

Sodium behaves similarly with these hydrocarbons and also with thionaphthen (Schönberg, Petersen, and Kaltschmitt, *Ber.*, 1933, **66**, 234).

In the experiments here described the exclusive *o*-substitution may be connected with the formation of the complex $\begin{matrix} C_6H_5 \\ R \end{matrix}\!\!>\!O \rightarrow Mg\!<\!\!\begin{matrix} Br \\ R' \end{matrix}$ which has been shown to break down in two ways,



The first is that established by Grignard, Späth and others (*loc. cit.*). The second type of decomposition, described in this communication, might favour *o*-substitution.

As similar addition products are probably formed in the case of the dialkylanilines, the interaction of ethylmagnesium bromide with boiling dimethylaniline was investigated. Treatment of the product with carbon dioxide at the ordinary temperature gave dimethylanthranilic acid. *p*-Dimethylaminobenzoic acid was not isolated, although this compound was obtained in several experiments by Houben and Freund (*Ber.*, 1909, **42**, 4815) from magnesium, methyl iodide, and boiling dimethylaniline, followed by heating in carbon dioxide, in some cases, under pressure. In two cases methylanthranilic acid was suspected by these authors but not isolated. Using monoethylaniline, ethyl iodide, and magnesium at the boiling point, and treating the product with carbon dioxide under pressure, they obtained *p*-diethylaminobenzoic acid and monoethylanthranilic acid. The formation of the latter compound was presumably due to the isomerisation of $C_6H_5{\cdot}NEt{\cdot}MgBr$ or of $C_6H_5{\cdot}NEt{\cdot}CO{\cdot}O{\cdot}MgBr$, a reaction entirely different from that occurring with diethylaniline.

These results form an interesting parallel to those of Morton and Hechenbleikner (*J. Amer. Chem. Soc.*, 1936, **58**, 2599). By heating *n*-amyl chloride and sodium with ligroin and (i) anisole and (ii) dimethylaniline, and treating the product with carbon dioxide, they obtained *o*-methoxybenzoic and dimethylanthranilic acids in minimum yields of 20 and 18%: $MeO{\cdot}C_6H_5 + NaC_5H_{11} \longrightarrow C_5H_{12} + MeO{\cdot}C_6H_4Na$. No mention of the *p*-isomers is made. Substitution by Na and by MgBr would appear, therefore, to take a similar course in anisole and dimethylaniline as well as in the compounds enumerated above.

Apparently the only other recorded instance of exclusive *o*-substitution in anisole and phenetole is their nitration by means of benzoyl nitrate (Francis, *Ber.*, 1906, **39**, 3801).

Although the results here described were obtained with ethyl- and *n*-propyl-magnesium bromides, it is suggested that hot anisole and phenetole should not be used as solvents for methylmagnesium iodide in the determination of active hydrogen by the Zerewitinoff reaction.

## Experimental.

*2-Thienylmagnesium Bromide and Phenetole.*—A solution of magnesium (1·5 g.) and 2-bromothiophen (10 g.) in ether (100 c.c.) was prepared in an atmosphere of nitrogen, sulphur (4 g.) and phenetole (30 c.c.) added, and the stirring and slow nitrogen stream continued overnight. The ether was then removed, and the residue heated at 200—205° for 6 hours in nitrogen, cooled in ice and salt, acidified with hydrochloric acid (some hydrogen sulphide being evolved), and extracted with ether. The combined extracts were shaken with aqueous sodium

hydroxide, and the ethereal layer (A) separated from the alkaline solution (B). Removal of ether from (A) and distillation of the phenetole in steam left a dark oil (3 c.c., $A_1$), which appeared to be a polysulphide.

Acidification of (B) yielded an oil containing a thiol, most of which formed a tar on distillation, but a few drops came over at 70°/18 mm. This and the residue were re-united and mixed with $A_1$, and the whole reduced with zinc dust and dilute hydrochloric acid, distilled in steam, and extracted with ether. The yellow oil so obtained was separated from a few white crystals, m. p. 215—216° (too small in amount for further examination), and distilled at the ordinary pressure, about 0·5 c.c. being collected from 160—200°. This unpromising material contained a thiol, recognised by its odour and reaction with mercury salts. In the belief that it might contain the desired thiophen-2-thiol it was dissolved in sodium hydroxide solution (10 c.c.), mixed with chloroacetic acid (0·5 g.) in water (1 c.c.), warmed, and left overnight. The precipitated sodium salt was washed with ether and acidified. On cooling, an acid separated, m. p. 64—65° after recrystallisation from hot water. It was free from halogen, gave no indophenin reaction, and depressed the m. p. of phenylthiolacetic acid, m. p. 61—62° (the desired 2-thienylthiolacetic acid was not available) (Found: C, 56·0; H, 5·6; S, 14·7. $C_2H_5·O·C_6H_4·S·CH_2·CO_2H$ requires C, 56·6; H, 5·7; S, 15·1%).

(I) *Ethylmagnesium Bromide and Phenetole.*—Magnesium (2 g.) and ethyl bromide (9 g.) were dissolved in ether (120 c.c.), phenetole (25 g.) added, the ether removed, and the residue heated at about 200° for 5 hours under reflux, some white fumes being observed during the first hour. The residue was then treated with ether and mercuric bromide (20 g.) in portions, the mixture boiled for 30 minutes, the ether removed, and water added. The residue was washed with hot water and extracted with acetone, which yielded 8 g. of a solid, m. p. 112—115°. This was twice recrystallised from aqueous acetone, once from benzene and once from aqueous alcohol. On each occasion the m. p. was 118° (Found: Hg, 50·3. Calc. for $C_8H_9OBrHg$: Hg, 50·0%). *o*-Phenetylmercury bromide melts at 121° (Michaelis, *loc. cit.*).

1 G. was boiled with potassium iodide (3 g.) in alcohol (50 c.c.) for 1 hour and diluted with water, giving an oil (0·3 g.) which solidified below 0°, m. p. 75—77°. Three recrystallisations from alcohol gave a halogen-free product, m. p. 82—83°. This is the m. p. recorded by Dimroth (*Ber.*, 1899, **32**, 758) for di-*o*-phenetylmercury, whereas Whitmore and Middleton (*J. Amer. Chem. Soc.*, 1923, **45**, 1753) give m. p. 81°. The values given by Michaelis (*loc. cit.*) for the m. p.'s of *p*-phenetylmercury bromide and di-*p*-phenetylmercury are 241·5° and 135°.

The aqueous filtrate from the crude *o*-phenetylmercury bromide contained the excess of phenetole and phenol.

(II) n-*Propylmagnesium Bromide and Anisole.*—The procedure was as described in (I), the quantities being: magnesium (2 g.), *n*-propyl bromide (11 g.), ether (100 c.c.), anisole (20 g.). After heating at 180—190° for 4 hours, gas being evolved, ether and mercuric bromide (20 g.) were added. Extraction with water, followed by alcohol, left some mercurous bromide and yielded 1 g. of *o*-anisylmercury bromide as a white solid, m. p. 186—187°, which was unaltered by two further crystallisations from aqueous acetone (Found: Hg, 52·3. Calc. for $C_7H_7OBrHg$: Hg, 51·8%).

The formation of phenol was demonstrated by conversion into tribromophenol, m. p. 95—96°. Yield, 24 g. This represented 87% of the weight (27·5 g.) to be expected if the whole of the propylmagnesium bromide had been used in demethylation (see p. 895).

(III) *Ethylmagnesium Bromide and Anisole.*—Quantities: Ethyl bromide (55 g.), magnesium (11·7 g.), ether (400 c.c.), anisole (140 g.). After removal of the ether the residue was heated at 180° for over 8 hours. Ether was again added, and the mixture divided into two parts, to one of which (C) was added mercuric chloride (30 g.) and to the other (D) mercuric bromide (40 g.), after which the mixtures were refluxed for an hour. Treatment with cold and then boiling water, followed by extraction with acetone–benzene, gave 7 g. of a solid which after three crystallisations from the same mixture melted at 186—186·5° alone and in admixture with the product, m. p. 186—187°, obtained from (D) below or with authentic *o*-anisylmercury bromide (see p. 898).

The pure product from (C) was therefore *o*-anisylmercury bromide; the crude product probably contained some chloride.

From (D) 11 g. of *o*-anisylmercury bromide, m. p. 186—187°, were similarly obtained. Two recrystallisations from acetone–benzene did not alter the m. p.

Mixed m. p.'s of (C) with ethylmercury chloride and ethylmercury bromide (m. p.'s 191—192° and 190°), obtained as below, both showed depressions to 170—175°.

*Confirmation of the Formation of* o-*Anisylmercury Bromide.*—(a) o-*Anisylmercury iodide.*

The *o*-anisylmercury bromide obtained in (III) (3·5 g.) was refluxed for 18 hours with potassium iodide (5 g.) in alcohol (50 c.c.). The mixture was then evaporated to half its bulk and water added. The precipitated solid (3·5 g.) had m. p. 165—166°, unchanged on recrystallisation from alcohol. *o*-Anisylmercury iodide melts at 165° and the *p*-compound at 227° (Michaelis, *Ber.*, 1894, **27**, 257).

(b) *Di-*o*-anisylmercury.*—*o*-Anisylmercury iodide (3·3 g.), sodium iodide (5 g.), and acetone (50 c.c.) were refluxed for 10 hours, and the solution concentrated to 25 c.c. and diluted with water. Below 0° a solid (1 g., m. p. 103—104°) was deposited; after two recrystallisations from alcohol this formed long needles, m. p. 108—108·5°. Michaelis (*loc. cit.*) and Whitmore and Middleton (*loc. cit.*) give m. p. 108°. The *p*-compound melts at 202° (Michaelis, *loc. cit.*).

(c) o-*Anisylmercury chloride.* Di-*o*-anisylmercury (0·2 g.) as obtained in (b) was boiled with mercuric chloride (0·5 g.) in alcohol for 30 minutes. Water precipitated a solid which, after washing with boiling water, melted at 176—177°. Recrystallisation from chloroform–ligroin gave a product, m. p. 177—178°. Michaelis (*loc. cit.*) gives m. p. 173—174°, but Whitmore and Middleton (*loc. cit.*) found m. p. 177—178° for *o*-anisylmercury chloride. Nesmejanow (*Ber.*, 1929, **62**, 1015) gives m. p. 180—181°.

*Reaction of Ethylmagnesium Bromide and Anisole under Various Conditions.*—An attempt was made to increase the formation of the intermediate *o*-anisylmagnesium bromide by using 55 g. of anisole instead of 140 g. as in the last experiment. After 1 hour's refluxing at 180° an explosion occurred.

When 140 g. of anisole were used and other ingredients as before, but heating for only 1½ hours, very little reaction occurred. Division into two parts (E and F), followed by addition of mercuric chloride and bromide, yielded in (E) ethylmercury chloride, mixed m. p. 191—192° with an authentic specimen of the same m. p. From (F) ethylmercury bromide was obtained, m. p. 190° (Marvel, Gauerke, and Hill, *J. Amer. Chem. Soc.*, 1925, **47**, 3009, give m. p. 193—195°), which depressed the m. p. of ethylmercury chloride to 160—162°.

In order to determine whether a higher temperature during the reaction between anisole and ethylmagnesium bromide would give rise to *p*-substitution, these substances, after being freed from ether, were heated in sealed tubes at 200° and 250° for 8 hours. The relative proportions were as in (D) on p. 897. Much gas was evolved when the tubes were opened. On addition of ether and mercury bromide no organo-mercury compound was formed. Distillation in steam gave an oil which appeared to contain phenol, bromophenols, and bromoanisoles.

o-*Anisylmercury Bromide and Bromine.*—The mercury compound was warmed with bromine water, giving 2 : 4 : 6-tribromoanisole, m. p., after crystallisation from alcohol, and mixed m. p. 85—88°.

o-*Anisylmercury Bromide from* o-*Anisidine.*—This preparation was analogous to that of the corresponding chloride (Nesmejanow, *Ber.*, 1929, **62**, 1015), employing method II (*ibid.*, p. 1012). Using *o*-anisidine (6·2 g.), ether (50 c.c.), mercuric bromide (18 g.), hydrobromic acid (*d* 1·49; 20 c.c.), and sodium nitrite (5 g.), we obtained the ***diazonium mercuritribromide*** as a red solid, which, after being washed with water, alcohol and ether, became greyish-white. Yield 20 g., m. p. 105—106°. It could be recrystallised from boiling water, giving a constant m. p. 117—118°, although much tar was formed (Found: N, 5·0. $CH_3{\cdot}O{\cdot}C_6H_4N_2{\cdot}HgBr_3$ requires N, 4·9%). The stability of this type of compound is remarkable. It readily couples, however, with an alkaline solution of β-naphthol.

The double salt was converted into *o*-anisylmercury bromide by boiling 9 g. with copper bronze (2 g.) in alcohol (70 c.c.), and filtering and concentrating the solution. A reddish solid separated, which was recrystallised from benzene (m. p. 178—180°) and twice from chloroform; it then melted at 186°, alone and in admixture with *o*-anisylmercury bromide, m. p. 186°, prepared from *o*-anisylmagnesium bromide (Found: C, 21·7; H, 2·2. Calc.: C, 21·7; H, 1·8%).

o-*Anisylmercury Bromide from the Grignard Reaction.*—A solution of magnesium (3 g.) and *o*-bromoanisole (25 g.) in ether (100 c.c.) was boiled with mercuric bromide (22 g.). After removal of ether and addition of water, the solid was washed with dilute hydrochloric acid and with boiling water, and extracted with chloroform. This deposited white crystals, m. p. 183—184°, *rising to 186° (constant) on one further crystallisation.*

p-*Anisylmercury Bromide from* p-*Anisidine.*—This was prepared by the method (I) described by Nesmejanow (*loc. cit.*, pp. 1013, 1015) for the *p*-phenetyl compound. Quantities: *p*-Anisidine (6 g.), hydrobromic acid (*d* 1·49; 70 c.c.), water (160 c.c.), sodium nitrite (4 g.). The diazonium salt was added to mercuric bromide (20 g.) in hydrobromic acid (*d* 1·49; 20 c.c.) and (20 g.). The diazonium double salt was washed with water, alcohol, and ether; m. p. 138—

139° [Found: Hg, 24·9; N, 7·6. Calc. for $(CH_3\cdot O\cdot C_6H_4N_2)_2HgBr_4$: Hg, 25·4; N, 7·1%]. The composition is not analogous to that of the corresponding *o*-derivative (see p. 898), but Nesmejanow (*loc. cit.*, p. 1012) refers to the difference in composition of the diazonium mercury halides which is observed on slightly altering the conditions of preparation.

The double salt (10·5 g.) was warmed with copper bronze (2·5 g.) and alcohol (50 c.c.), left for 24 hours, and the alcohol evaporated. Extraction of the residue with acetone–benzene gave a deposit, m. p. 243—244°. It did not depress the m. p. 241—242° of a specimen obtained from *p*-bromoanisole (see below) (Found: C, 22·0; H, 2·1. Calc.: C, 21·7; H, 1·8%).

p-*Anisylmercury Bromide from* p-*Bromoanisole.*—Magnesium (3·8 g.) and *p*-bromoanisole (30 g.), dissolved in ether (100 c.c.), were treated with mercuric bromide (30 g.). After heating under reflux, the ether was removed, water added, and the solid washed with ether, boiled with water, and extracted with hot acetone–benzene. The deposit, crystallised four times from the same solvent, melted at 241—242°.

*Action of Dimethylaniline on Ethylmagnesium Bromide.*—A solution of ethyl bromide (9 g.) and magnesium (2 g.) in ether (120 c.c.) was treated with dimethylaniline (25 g.), and the ether removed. The residue was boiled under reflux for 5 hours and cooled, and, after addition of ether (200 c.c.), dry carbon dioxide was passed through, with stirring and cooling for about 2 hours. The product was dissolved in ammonium chloride solution and extracted twice with ether, and the aqueous layer acidified with acetic acid. There was no precipitate, indicating absence of *p*-dimethylaminobenzoic acid. The solution was then evaporated, and the residue extracted with boiling ether. The ether yielded dimethylanthranilic acid, m. p., after two crystallisations from ether, and mixed m. p. 70—71°.

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The University, Leeds. [*Received, March 14th*, 1938.]

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## 174. *Aromatic Hydroxy-sulphones.*

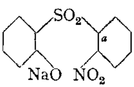
By Mollie E. Heppenstall and Samuel Smiles.

It is shown that the sodium salts of aromatic *o*-hydroxy-sulphones may be obtained in the covalent state. This tendency of sulphonyl to acquire alkali metal is evidently an important factor in promoting the intramolecular displacement of sulphonyl by phenoxyl in the rearrangement of 2-hydroxydiphenylsulphones. Examination of *o*-, *m*-, and *p*-hydroxy-derivatives of diphenyl- and phenylmethyl-sulphones has shown that the *o*- and *p*-series are distinguished by the formation of hydrates of varying stability; the character of these is discussed. 2 : 4-*Bismethylsulphonylphenol* is easily obtained from sodium hydroxide and 1-*chloro*-2 : 4-*bismethylsulphonylbenzene*; quantitative measurements showed that the reactivity of halogen in the latter is of the same order as that in 1-chloro-2 : 4-dinitrobenzene.

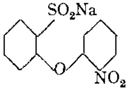
It has been shown that 2′-nitro-2-hydroxydiphenylsulphones (*e.g.*, as I) are converted in alkaline media (J., 1934, 422) into the sulphinic acids (*e.g.*, II), sulphonyl being displaced by phenoxyl. With sulphones containing sufficiently active hydroxyl this type of displacement takes place exclusively, but in cases where formation of the sulphinic acid proceeds slowly owing to restricted activity of the phenolic hydroxyl the accompanying formation of small amounts of the thioxin derivative (III) by displacement of the nitro-group may be detected. This preference for displacement of sulphonyl in sulphones of type (I) forms an interesting contrast with the intermolecular attack of alkaline agents on derivatives of *o*-nitro-sulphones such as (IV), which, as Loudon and his colleagues (*e.g.*, Loudon and Robson, J., 1937, 244) have shown, leads in most cases to a preferential displacement of the nitro-group.

In these cases of intramolecular rearrangement (I ⟶ II) it is evident that displacement of sulphonyl may obtain preference from the more favourable situation of the phenolic ion with respect to the carbon atom *a* than to that bearing the nitro-group. There is, however, another factor to be considered. The capture of sodium by oxygen

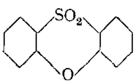
of the displaced group is an important stage in the process and a predisposition of either nitroxyl or sulphonyl to this action would evidently favour the displacement of the group concerned. The question then arises whether nitroxyl or sulphonyl in a sulphone such as (I) is capable of behaving in this manner and, if so, whether there is likely to be sufficient difference in their behaviour to give preference to one or other of the possible types of product (II or III). Some evidence of the tendency of a nitro-group to acquire alkali metal exists in the formation of covalent alkali derivatives of *o*-nitrophenols (Sidgwick and Brewer, J., 1925, **127**, 2385), but, although nothing is yet known of the behaviour of nitrophenols of the type (I) now in question, it may be assumed that the nine-membered ring required for the formation of a covalent derivative would be attained only with difficulty.



(I.)

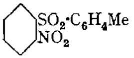


(II.)

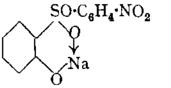


(III.)

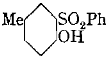
There is no previous evidence available to show whether sulphonyl in *o*-hydroxy-sulphones is capable of acquiring alkali metal as shown in (V); experiments now described provide the required information and show that covalent alkali derivatives of this type are readily formed. Accordingly it is suggested that at least a secondary factor in favour of displacement of sulphonyl in (I) ⟶ (II) is to be found in the proximity of this group to the phenoxide, which enables it to acquire the alkali metal of the latter more readily than the less favourably placed nitro-group. The covalent sodium derivatives of *2-hydroxydiphenylsulphone* and related compounds have the usual properties of this class of substance; many of those examined are remarkable for their greater solubility in cold than in hot chloroform; the property has been used for their purification and evidently depends on the instability of hydrates in the boiling solvent. The fact that the anhydrous substances may be obtained indicates the occurrence of the alkali metal in the 2-covalent state, but in presence of moisture there is no doubt that a higher covalency is attained. Some of these sulphones, *e.g.*, (VI), showed a tendency to yield derivatives of bimolecular " acid " type, evidently containing the four-covalent metal; in fact in this case (VI) the normal derivative was not observed. With the di-*o*-hydroxy-sulphone (VII) the existence of a covalent disodium derivative would require the formation of a spirocyclic system, but attempts to obtain this substance were unsuccessful, the monosodium compound being always obtained. Analytical data cannot decide whether this product is derived from the bimolecular acid type containing the



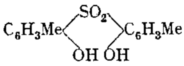
(IV.)



(V.)



(VI.)

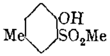


(VII.)

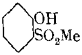
disodium derivative, but the fact that the monomethyl ether of (VII) gave a normal sodium derivative possessing properties similar to those of the product in question indicates an analogous structure for the latter. It is worth notice that the covalent state of these derivatives appears to be less stable than that of the sodium derivatives of *o*-hydroxy-ketones or -aldehydes. For example, they are decomposed by salicylaldehyde, are readily methylated in cold aqueous solution (see also Price and Smiles, J., 1928, 3156), and in alcoholic solution react normally with 2 : 4-dinitrochlorobenzene in contrast with the behaviour of sodium salicylaldehyde (Brady, J., 1932, 352).

In the course of these experiments the monohydroxy-derivatives of diphenylsulphone and phenylmethylsulphone were examined. The *o*- and *p*-compounds in each series are characterised by the formation of monohydrates and are thus distinguished from the *m*-derivatives, which were obtained only in the anhydrous state. The hydrates in

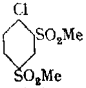
question show varying stability; most of them yield the anhydrous phenol when they are heated and dissolve in hot benzene with separation of water; but (VIII) yields the hydrate when exposed to air, and the hydrate of (IX) is the most stable of the series, attempts to obtain the anhydrous phenol being unsuccessful. From the fact that the



(VIII.)



(IX.)



(X.)

hydrate of (IX) dissolves in hot benzene without separation of water it is concluded that the water in these hydrates is covalently bound. It may then be enquired whether the water of hydration is associated with hydroxyl or sulphonyl; all available evidence is contrary to the latter alternative. The tendency of sulphonyl oxygen in sulphones to form co-ordinated adducts is not great and is noticeably less than that of carbonyl oxygen; in fact at present the only undoubted evidence of it is in the sodium derivatives of *o*-hydroxy-sulphones now recorded. The addition of aluminium chloride to aromatic sulphones has been observed (Olivier, *Chem. Weekblad*, 1914, **11**, 372), but it is uncertain whether the benzene nucleus or sulphonyl is concerned in the formation of these products. Moreover, attempts to obtain boroacetates from the *o*-hydroxy-sulphones have been unsuccessful and the formation of hydrochlorides or perchlorates from the *o*- and *p*-derivatives and their methyl ethers could not be detected. In view of these facts and the circumstance that the methyl ethers do not form stable hydrates the hydration water may be regarded as associated with hydroxyl, but at present no adequate explanation can be given of the varying stability of the hydrates or of the exceptional behaviour of the *m*-derivatives.

In other experiments concerning the intramolecular displacement of an aromatic nucleus containing positive substituents it was found that the presence of the nitro-group led to experimental difficulties. Since the use of the methylsulphonyl group for establishing the required positive condition of the nucleus appeared likely to be an advantage owing to its stability in presence of reducing agents, the preparation of 2 : 4-*bismethylsulphonylphenol* has been more fully studied. In this connexion it is worth notice that, whilst Todd and Shriner (*J. Amer. Chem. Soc.*, 1934, **56**, 1382) have shown that the activity of halogen in *o*- or *p*-chlorophenylmethylsulphone is much more feeble than that in *o*- and *p*-chloronitrobenzene, the activity of halogen in 1-*chloro*-2 : 4-*bismethylsulphonylbenzene*, as determined by quantitative measurement, is somewhat less than but of the same order as that in 1-chloro-2 : 4-dinitrobenzene. In fact the phenol may be obtained in high yield from the reaction of alkali hydroxide with (X), and similar reagents such as aniline, piperidine, sodium ethoxide, sodium thiophenoxide, sulphinate, and sodium sulphide yielded corresponding derivatives by displacement of the halogen.

## Experimental.

2-Hydroxydiphenylsulphone was prepared by Ullmann's method (*Ber.*, 1901, **34**, 1153) from 2-nitrodiphenylsulphone. Reduction of the latter was best effected by shaking it with acetic acid which had been saturated with hydrogen chloride and contained the theoretical amount of stannous chloride. The sparingly soluble stannichloride of 2-aminodiphenylsulphone was decomposed by water and yielded the base in a sufficiently pure condition for diazotisation (Ullmann, *loc. cit.*). The phenol was purified from dilute acetone; the *monohydrate* thus obtained had m. p. 82° (Found : C, 57·4; H, 4·8. $C_{12}H_{10}O_3S,H_2O$ requires C, 57·1; H, 4·8%). Ullmann (*loc. cit.*) records this m. p. for a material described as the anhydrous phenol. The latter was obtained from the hydrate by drying over phosphoric oxide under diminished pressure at 78°; it had m. p. 97° (Found : C, 61·2; H, 4·5. $C_{12}H_{10}O_3S$ requires C, 61·5; H, 4·3%). The hydrate dissolved in hot benzene with separation of water. The phenol was readily methylated by methyl sulphate in presence of cold dilute sodium hydroxide solution. 2-*Methoxydiphenylsulphone* formed prisms, m. p. 143°, from alcohol (Found : C, 62·8; H, 5·0. $C_{13}H_{12}O_3S$ requires C, 62·9; H, 4·8%). With boroacetic anhydride under usual conditions

2-*acetoxydiphenylsulphone* was obtained; this formed plates, m. p. 84°, from alcohol (Found: C, 61·2; H, 4·5. $C_{14}H_{12}O_4S$ requires C, 60·9; H, 4·3%). The *sodium* derivative was prepared from the phenol and sodium ethoxide in alcohol. The residue obtained after removal of the solvent was extracted with chloroform (Soxhlet), the product being collected from the hot medium. It formed needles, m. p. 290—293° (Found: Na, 8·9. $C_{12}H_9O_3SNa$ requires Na, 9·0%). These dissolved in cold chloroform and separated when the solution was boiled.

3-*Hydroxydiphenylsulphone*.—3-Nitrodiphenylsulphone (Olivier, *Rec. Trav. chim.*, 1916, **35**, 110) was reduced in alcohol with stannous chloride and hydrochloric acid. The alcohol was removed and the base, liberated from the residual aqueous solution, was purified from benzene. 3-*Aminodiphenylsulphone* formed plates, m. p. 117° (Found: N, 6·0. $C_{12}H_{11}O_2NS$ requires N, 6·0%). The base, after diazotisation in 60% sulphuric acid, yielded the required phenol, which separated from water or aqueous alcohol in needles, m. p. 163° (Found: C, 61·2; H, 4·1. $C_{12}H_{10}O_3S$ requires C, 61·5; H, 4·3%). The formation of a stable hydrate was not detected. 3-*Methoxydiphenylsulphone* formed needles, m. p. 90·5°, from alcohol (Found: C, 62·4; H, 4·4. $C_{13}H_{12}O_3S$ requires C, 62·9; H, 4·8%).

4-*Hydroxydiphenylsulphone*.—4-Nitrodiphenylsulphone (Ullmann, *loc. cit.*) was conveniently obtained by heating (180°) 4-chloronitrobenzene and potassium benzenesulphinate in ethylene glycol. Reduction of the nitro-derivative and conversion of the amine into the phenol were effected as in the case of the *o*-derivative. The phenol separated from dilute alcohol as the *monohydrate* (Found: C, 57·0; H, 4·9. $C_{12}H_{10}O_3S,H_2O$ requires C, 57·1; H, 4·8%), which dissolved in hot benzene with separation of water. Dehydration in a vacuum (118°, phosphoric oxide) yielded the anhydrous phenol, m. p. 137°. This substance has been obtained by Steinkopf (*J. pr. Chem.*, 1927, **117**, 60) and by Hilbert and Johnson (*J. Amer. Chem. Soc.*, 1929, **51**, 1526), using other methods, but these authors did not observe the formation of a hydrate. The methyl ether had m. p. 90° (also Hilbert and Johnson, *loc. cit.*).

2-*Methoxy-5-methyldiphenylsulphone* (as VI).—Aluminium chloride (18 g.) was added to a solution of 2-methoxy-5-methylbenzenesulphonyl chloride (20 g.) in benzene (100 c.c.). Subsequently (3 hrs., 15°) water was added, the excess of benzene removed by steam, and the non-volatile *sulphone* purified from alcohol; it formed plates, m. p. 140° (Found: C, 64·6; H, 5·2. $C_{14}H_{14}O_3S$ requires C, 64·1; H, 5·3%).

2-*Hydroxy-5-methyldiphenylsulphone* (VI).—The methyl ether (5 g.) was heated (4 hrs., 180°) with hydrobromic acid (10 c.c., *d* 1·7); the product was purified from dilute acetone. The *monohydrate* thus obtained formed needles, which were stable in moist air (Found: C, 58·5; H, 5·3. $C_{13}H_{12}O_3S,H_2O$ requires C, 58·6; H, 5·3%), but lost water at temperatures below its m. p. The anhydrous *phenol* had m. p. 139° (Found: C, 62·7; H, 4·8. $C_{13}H_{12}O_3S$ requires C, 62·9; H, 4·7%). The substance was readily methylated in dilute aqueous alkaline solution. The *sodium* derivative was obtained by evaporating an alcoholic solution of the sulphone (1 mol.) and sodium hydroxide (1 mol.) and crystallising the residue from moist chloroform; it formed needles, m. p. 260° (Found: Na, 4·3. $C_{13}H_{12}O_3S,C_{13}H_{11}O_3SNa$ requires Na, 4·4%). The same substance separated when alcoholic sodium ethoxide (0·5 mol.) was added to an alcoholic solution of the phenol (1 mol.) (Found: Na, 4·5%). The substance was soluble in warm chloroform and separated therefrom either in needles or in the colloidal state, the whole then forming a transparent jelly.

5-*Chloro-2-methoxydiphenylsulphone* was obtained by the interaction of 5-chloro-2-methoxybenzenesulphonyl chloride and benzene in presence of aluminium chloride (4 hrs., 40°); isolated in the usual way and purified from alcohol, it had m. p. 144° (Found: C, 55·1; H, 3·9. $C_{13}H_{11}O_3ClS$ requires C, 55·2; H, 3·9%). When heated with hydrobromic acid, it yielded 5-*chloro-2-hydroxydiphenylsulphone*, which crystallised from chloroform–light petroleum in needles, m. p. 139° (Found: C, 53·1; H, 3·1. $C_{12}H_9O_3ClS$ requires C, 53·6; H, 3·3%). The existence of a hydrate was not observed. Aqueous alkaline methylation readily gave the methyl ether, and the *acetyl* derivative, m. p. 134° (Found: C, 53·9; H, 3·8. $C_{14}H_{11}O_4ClS$ requires C, 54·1; H, 3·5%), was formed by treatment with boroacetic anhydride under the usual conditions. The 2 : 4-*dinitrophenyl* ether was formed in good yield during the reaction of the sodium salt with 2 : 4-dinitrochlorobenzene in hot alcohol; purified from acetic acid, it formed needles, m. p. 187° (Found: N, 6·7. $C_{18}H_{11}O_7N_2ClS$ requires N, 6·4%). The *sodium* derivative was obtained by evaporating an alcoholic solution of the sulphone (1 mol.) and sodium ethoxide (1 mol.). The residue was insoluble in water and contained the "acid" salt and the normal sodium derivative. The latter was readily removed by warm chloroform, from which it separated in needles, m. p. 247° (Found: Na, 8·0. $C_{12}H_8O_3ClSNa$ requires Na, 7·9%), sparingly soluble in hot toluene. The *lithium* derivative was obtained by evaporating

an alcoholic solution of the phenol (1 mol.) and lithium hydroxide (1 mol.); it was extracted from the mass by hot chloroform and separated from the cold medium in needles, m. p. 198°. These evidently consisted of the *dihydrate* (Found: H, 3·5. $C_{12}H_8O_3ClSLi,2H_2O$ requires H, 3·8%), but they lost water in a vacuum at 118° (phosphoric oxide) (Found: Li, 2·5; H, 2·9. $C_{12}H_8O_3ClSLi$ requires Li, 2·5; H, 2·9%).

2 : 2′-Dihydroxy-5 : 5′-dimethyldiphenylsulphone (Tassinari, *Gazzetta*, 1889, **19**, 346) was best prepared by oxidising the sulphoxide (J., 1910, **97**, 2248) with hydrogen peroxide (3 mols.) in hot acetic acid (100°, 3 hrs.). Reaction with boroacetic anhydride yielded the *diacetyl* derivative, m. p. 211° (Found: C, 59·6; H, 5·1. $C_{18}H_{18}O_6S$ requires C, 59·7; H, 5·0%). The *sodium* derivative was prepared from an alcoholic solution of the sulphone (1 mol.) and sodium ethoxide (1 mol.). The residue obtained after removal of the solvent was extracted with chloroform (Soxhlet), the crystalline product being collected from the hot liquid. It formed needles, m. p. 190° after being dried (118°, phosphoric oxide) in a vacuum (Found: Na, 7·7. $C_{14}H_{13}O_4SNa$ requires Na, 7·7%). The substance was decomposed by salicylaldehyde, yielding the sodium derivative of the latter.

*2-Hydroxy-2′-methoxy-5 : 5′-dimethyldiphenylsulphone.*—*O*-Carbethoxy-*p*-cresol-3-sulphonyl chloride (Bennett, Lesslie, and Turner, J., 1937, 445) was added (21 g.) to *p*-tolyl methyl ether (36 g.) containing aluminium chloride (21 g.), and the mixture warmed (40—50°) until liberation of hydrogen chloride had ceased (18 hrs.). After the excess of the ether had been removed in steam the residue was hydrolysed by hot alcoholic sodium hydroxide. The product, isolated in the usual way, formed prisms, m. p. 153°, from alcohol (Found: C, 62·0; H, 5·8. $C_{15}H_{16}O_4S$ requires C, 61·6; H, 5·5%). The *sodium* derivative formed needles from alcohol; these were soluble in chloroform and sparingly so in warm benzene or toluene and had m. p. 219° (Found: Na, 7·5. $C_{15}H_{15}O_4SNa$ requires Na, 7·5%). The *lithium* derivative was prepared from the sulphone and lithium hydroxide in alcohol; it was purified by addition of light petroleum to a chloroform solution (Found: Li, 2·4; H, 5·3. $C_{15}H_{15}O_4SLi$ requires Li, 2·3; H, 5·0%).

*2-Methoxyphenylmethylsulphone* (compare IX), obtained by methylating anisole-2-sulphinic acid, formed plates, m. p. 95°, from water (Found: C, 51·3; H, 5·5. $C_8H_{10}O_3S$ requires C, 51·6; H, 5·4%). When it was heated (4 hrs., 150°) with hydrobromic acid (*d*, 1·7), it was demethylated; addition of water to the solution yielded the *hydrate* of *2-hydroxyphenylmethylsulphone*. This was purified from hot water and formed prisms, m. p. 87·5°, which were soluble in benzene (Found: C, 44·6; H, 5·6. $C_7H_8O_3S,H_2O$ requires C, 44·2; H, 5·3%). An alcoholic solution gave a deep red colour with ferric chloride. Complete dehydration of the phenol was not effected after 8 weeks in a vacuum (15°, phosphoric oxide); a sample containing about 5% of the hydrate had m. p. 67° (appxt.).

3-Aminophenylmethylsulphone was obtained by reducing 3-nitrophenylmethylsulphone (J., 1925, **127**, 1249) with tin and hydrochloric acid. The base, isolated in the usual manner, separated from hot water in plates, m. p. 58°. Zincke (*Ber.*, 1913, **46**, 782) obtained this substance by oxidising 3-acetamidophenyl methyl sulphide and deacetylating the product and gave the m. p. 72° and that of the acetyl derivative as 137°. The acetyl derivative of the base, m. p. 58°, had m. p. 137° (Found: N, 6·7. Calc.: N, 6·6%) and yielded the original base (m. p. 58°) on deacetylation.

*3-Hydroxyphenylmethylsulphone* was obtained from the amino-derivative by diazotisation and was isolated from the solution obtained by extraction with chloroform. After purification (charcoal) it separated from benzene in needles, m. p. 82° (Found: C, 48·8; H, 5·0. $C_7H_8O_3S$ requires C, 48·8; H, 4·6%). The formation of a hydrate was not observed. Methylation in aqueous alkaline media yielded *3-methoxyphenylmethylsulphone*, which formed plates, m. p. 47°, from water (Found: C, 51·4; H, 5·6. $C_8H_{10}O_3S$ requires C, 51·6; H, 5·4%). This substance was also obtained from 3-methoxybenzenesulphinic acid, but the preparation of the phenol from it gave unsatisfactory results.

*4-Methoxyphenylmethylsulphone*, obtained from anisole-*p*-sulphinic acid, formed plates, m. p. 121°, from water (Found: C, 51·5; H, 5·7. $C_8H_{10}O_3S$ requires C, 51·6; H, 5·4%). Demethylation with hydrobromic acid yielded *4-hydroxyphenylmethylsulphone*, m. p. 94°, after being dried and purified from benzene (Found: C, 49·0; H, 4·8. $C_7H_8O_3S$ requires C, 48·8; H, 4·6%). It separated from water as the *hydrate*, m. p. 49° (Found: C, 44·5; H, 5·5. $C_7H_8O_3S,H_2O$ requires C, 44·2; H, 5·3%).

*2-Hydroxy-5-methylphenylmethylsulphone* (VIII) was obtained by demethylating 2-methoxy-5-methylphenylmethylsulphone (J., 1923, **123**, 2391) with hydrobromic acid; it separated from water as the *hydrate*, which formed thick needles, m. p. 78° (Found: C, 47·2; H, 6·1.

$C_8H_{10}O_3S,H_2O$ requires C, 47·1; H, 5·9%) and lost water in a vacuum at 50° (phosphoric oxide) (Found: $H_2O$, 8·7. Calc.: $H_2O$, 8·8%), yielding the anhydrous phenol, m. p. 89° (Found: C, 51·3; H, 5·2. $C_8H_{10}O_3S$ requires C, 51·6; H, 5·4%). The latter absorbed moisture from the atmosphere, yielding the hydrate.

*5-Chloro-2-hydroxyphenylmethylsulphone*, obtained from the methyl ether (*J.*, 1925, **127**, 2746) by demethylation, separated from water in plates, m. p. 140° (Found: C, 40·4; H, 3·2. $C_7H_7O_3ClS$ requires C, 40·7; H, 3·4%). No hydrate was obtained.

2 : 4-*Bismethylsulphonylanisole*.—2 : 4-Bischlorosulphonylanisole (Pollak, *Monatsh.*, 1928, **50**, 55) was converted into the disulphinic acid by reaction with sodium sulphite in concentrated neutral solution. The product was removed by ether from the acidified mixture and methylated as the potassium salt in boiling alcohol with methyl iodide; the required *disulphone*, isolated in the usual manner, formed stout needles, m. p. 197°, from acetic acid (Found: C, 40·9; H, 4·5. $C_9H_{12}O_5S_2$ requires C, 40·9; H, 4·5%), which were converted into the phenol by demethylation with hydrobromic acid. Since the yields of the hydroxy-sulphone by this method were very poor, an alternative route to the desired phenol was taken *via* the chloro-derivative (X).

1-Chloro-2-chlorosulphonyl-4-methylsulphonylbenzene was obtained by heating (7 hrs., 150—180°) a solution of 1-chloro-4-methylsulphonylbenzene (1 mol.) in chlorosulphonic acid (5 mols.); isolated in the usual manner and purified from benzene, it formed needles, m. p. 144°. These were converted into the *anilide*, m. p. 161° (from alcohol), for analysis (Found: C, 45·2; H, 3·6; N, 4·0. $C_{13}H_{12}O_4NClS_2$ requires C, 45·1; H, 3·4; N, 4·0%).

1-*Chloro*-2 : 4-*bismethylsulphonylbenzene* (X) was prepared from the foregoing sulphonyl chloride by two methods. (a) Reduction of the sulphonyl chloride with hydrogen iodide (5 mols., *d* 1·7) in acetic acid (100°, 30 mins.) gave a high yield of *di*-2-*chloro*-5-*methylsulphonylphenyl disulphide*, which formed needles, m. p. 253°, from acetic acid (Found: C, 37·5; H, 2·7. $C_{14}H_{12}O_4Cl_2S_4$ requires C, 37·9; H, 2·7%). This was further reduced by glucose (1 mol.) in warm aqueous alcohol containing sodium hydroxide (4 mols.) under usual conditions. After the alkaline solution of the thiol had been diluted with an equal volume of water and filtered, it was shaken with methyl sulphate. 1-*Chloro*-4-*methylsulphonyl*-2-*methylthiolbenzene* then separated; it formed needles, m. p. 107°, from alcohol (Found: S, 26·7. $C_8H_9O_2ClS_2$ requires S, 27·0%). When it was oxidised (100°, 1 hr.) in acetic acid (1 g. in 10 c.c.) with hydrogen peroxide (4 mols., 30%), the required disulphone (X) was obtained; the yield in this operation was poor (18%), the overall yield being correspondingly reduced. (b) Conversion of the sulphonyl chloride into the sulphinic acid by reduction with aqueous sodium sulphite was unsatisfactory and tedious, mainly owing to the high solubility of the acid in water, which rendered its isolation difficult. A more successful method of reduction and one which may be usefully applied to the preparation of other sulphinic acids was afforded by the reaction of the sulphonyl chloride with sodiomalonic ester. The finely powdered 1-chloro-2-chlorosulphonyl-4-methylsulphonylbenzene (1 mol.) was slowly added to a cold and stirred solution of ethyl sodiomalonate (2 mols.) in alcohol. After the mixture had been kept for 1 hour, the solvent was evaporated, water being added to the neutralised residue before extraction with ether. Evaporation of the aqueous solution gave a residue of the sodium sulphinate, which was methylated in boiling alcohol with methyl iodide, the *product* (X) being isolated in the usual manner; it had m. p. 187° after purification from acetic acid (Found: C, 35·8; H, 3·5. $C_8H_9O_4ClS_2$ requires C, 35·8; H, 3·3%).

2 : 4-*Bismethylsulphonylphenol*.—The chloro-derivative (X) was rapidly attacked by boiling aqueous or alcoholic sodium hydroxide; the *phenol* after being purified from hot water, formed clusters of needles, m. p. 220° (Found: C, 38·4; H, 3·9. $C_8H_{10}O_5S_2$ requires C, 38·4; H, 4·0%), which were soluble in aqueous sodium carbonate. When method (b) was used for the reduction of the sulphonyl chloride, 115 g. of chlorobenzene yielded 60 g. of the phenol. The activity of the halogen in 1-chloro-2 : 4-bismethylsulphonylbenzene (1) in boiling alcoholic sodium ethoxide is shown by the following data in comparison with that of the halogen in 1-chloro-2 : 4-dinitrobenzene (2) and 1-chloro-2-nitrobenzene (3); the method used was analogous to that of Todd and Shriner (*loc. cit.*). In 30 c.c. of boiling alcohol containing sodium ethoxide (0·286N) and the substance (0·005 mol.), after 15 minutes the % halogen removed was, with (1), 90·1 and, with (2), 97·6; with 0·125N-sodium ethoxide under the same conditions the % halogen removed was, with (1), 83·1, with (2), 95·5, and with (3), 16·3. Under these conditions 2 : 4-*bismethylsulphonylphenetole* was formed; it separated from alcohol in needles, m. p. 201° (Found: C, 42·8; H, 4·9. $C_{10}H_{14}O_5S_2$ requires C, 43·1; H, 5·0%). The chloro-disulphone (X) behaved similarly with other anionoid reagents. Boiling

aniline yielded 2 : 4-*bismethylsulphonyldiphenylamine*, which formed needles, m. p. 218°, from alcohol (Found: N, 4·3. $C_{14}H_{15}O_4NS_2$ requires N, 4·3%); piperidine (100°) gave (94%) N-2′ : 4′-*bismethylsulphonylphenylpiperidine*, m. p. 156° (Found: N, 4·4. $C_{13}H_{19}O_4NS_2$ requires N, 4·4%); sodium thiophenoxide in boiling alcohol gave (74%) 2 : 4-*bismethylsulphonyldiphenyl sulphide*, m. p. 232° (Found: C, 48·7; H, 4·0; S, 27·6. $C_{14}H_{14}O_4S_3$ requires C, 49·1; H, 4·1; S, 28·1%); and sodium benzenesulphinate in boiling ethylene glycol gave 2 : 4-*bismethylsulphonyldiphenylsulphone*, m. p. 270—271° (Found: C, 45·0; H, 3·7; S, 25·6. $C_{14}H_{14}O_6S_3$ requires C, 44·9; H, 3·7; S, 25·7%), which was also obtained by oxidising the sulphide with hydrogen peroxide in acetic acid.

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## 175. *Influence of Directing Groups on Nuclear Reactivity in Oriented Aromatic Substitutions. Part III. Nitration of Ethyl Benzoate.*

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In the discussion of aromatic substitution in Part I it was shown that directing substituents could be divided into four broad classes, differing in the mechanism of electronic interaction between the substituent and the ring, and observably distinguished by their effects on both the orientation and the velocity of substitution. The four classes are typically represented by toluene, ethyl benzoate, chlorobenzene and the phenoxide ion, severally: the substituent in each of these compounds modifies the reactivity of the available nuclear positions in a characteristic way. For a given substitution process, the effect of the original group can be represented by a set of factors expressing the ratios in which, for each nuclear position, the probability of substitution has been changed by the group.

In Part II such sets of factors were determined for the nitration of toluene, by reagents including acetyl nitrate in acetic anhydride, at 0° and at 30°. In this paper the same factors are determined for the nitration of ethyl benzoate by acetyl nitrate in acetic anhydride at 18°. In Part IV the work is extended to the halogenobenzenes.

The reported experiments include a determination by the competition method (the theory of which is discussed) of the ratio of the rates of nitration of benzene and of ethyl benzoate. The latter is nitrated 272 ± 6 times more slowly than the former. Another series of experiments is concerned with the determination of the proportions in which *o*-, *m*-, and *p*-nitro-isomerides are formed in the nitration of ethyl benzoate, with the reagent and temperature used in the rate experiments. The respective proportions are 24·1 ± 0·1, 72·0 ± 0·1, and 4·0 ± 0·1%.

From these results the factors referred to can be calculated. The carbethoxyl group in ethyl benzoate reduces the probability of substitution of each *o*-position by the factor 0·0026, of each *m*-position by the factor 0·0079, and of the *p*-position by the factor 0·0009. Thus just as the methyl substituent activates all positions, the *o*- and *p*-positions more than the *m*-, so the carbethoxyl group deactivates all positions, *o*- and *p*- more than *m*-. These relations are shown schematically at the end of the paper.

PART I of this series (Ingold and Shaw, J., 1927, 2918) was devoted to a general discussion of the laws of aromatic substitution by electrophilic reagents, and it was there pointed out that directing substituents can be divided into four broad classes, differing from one another in the mechanism of the electronic interaction between the group and the nucleus:

| | | | | |
|---|---|---|---|---|
| Class 1. | $\leftarrow$ R | Mechanism $+I$ | Example: | Toluene |
| ,, 2. | $\rightarrow$ R | ,, $-I$ | ,, | Ethyl benzoate |
| ,, 3. | $\rightarrow$ R (with curved arrow) | ,, $-I+T$ | ,, | Chlorobenzene |
| ,, 4. | $\leftarrow$ R (with curved arrow) | ,, $+I+T$ | ,, | Phenoxide ion |

It was shown both theoretically and practically that these four classes are distinguishable with respect to the observable phenomena of substitution if one takes account, not only of orienting action, but also of effects on rate of substitution. When we know the effect of a group, not only on the proportions in which isomeric substitution products are formed, but also on the speed of the total substitution, we have a measure of the extent to which that group has modified the reactivity of each of the available nuclear positions with respect to the substitution.

The next step was to obtain quantitative orientational and velocity data for a few important members of each of the four classes. For this purpose we considered the substitution of monosubstituted benzenes only, in order not to have to take account of the superposed effects of several groups. We selected nitration as the substitution to be studied owing to its wide applicability, and the circumstance that monosubstitution can be realised with less disturbance from polysubstitution in this than in most other reactions. An extensive mass of orientational data for the nitration of monosubstituted benzenes already exists, although we have had to supplement it. Our main task, however, was to supply the complementary velocity data.

This experimental programme was commenced with the work described in Part II (Ingold, Lapworth, Rothstein, and Ward, J., 1931, 1959). The example studied was toluene (Class 1). In this paper it is ethyl benzoate (Class 2). In Part IV it is the group of halogenobenzenes (Class 3).

As in the previous work on toluene, two groups of experiments are here recorded. In the first we measure by a competition method the ratio of the rates of mononitration of ethyl benzoate and of benzene. The reagent must be one which will form a homogeneous reaction mixture, since otherwise observed rates have no simple significance: we have employed as nitrating agent acetyl nitrate in acetic anhydride, *i.e.*, mixtures made from nitric acid and excess of acetic anhydride. It is this circumstance which necessitated the second group of experiments. Holleman determined the proportions in which isomerides are formed when ethyl benzoate is nitrated with nitric acid: we have carried out similar determinations for the reagent used in the rate experiments.

### (1) *Relative Rates of Nitration of Ethyl Benzoate and of Benzene with Acetyl Nitrate in Acetic Anhydride at* 18°.

The immediate object of the experiments was to determine the ratio in which ethyl nitrobenzoates (total) and nitrobenzene are formed when the nitrating agent competes for ethyl benzoate and benzene originally present in known proportions and both in large excess. In the present work the two aromatic compounds were always initially in equivalent proportions. For this case, the experimental ratio, $R$, in which the compounds are found to have undergone nitration is equal to the ratio of their specific rates of reaction $k_y/k_x$, in the limit of small amounts of nitration. If the quantity of either compound nitrated is not small in comparison with the amount originally present, then $R$ is only a first approximation to $k_y/k_x$, because, after the commencement of reaction, the two aromatic compounds get out of equivalence; the ratio $R$ can, however, be corrected to give $k_y/k_x$. The formula we use for this purpose is $k_y/k_x = \log(y/y_0)/\log(x/x_0)$, to which the first approximation is clearly $R = (y_0 - y)/(x_0 - x)$, where $x_0$ and $y_0$ are the initial concentrations of the aromatic compounds and $x$ and $y$ their concentrations when the reaction is stopped.

It is important to consider the conditions under which the correction formula is valid, because it cannot, of course, be derived without any kinetic assumptions. In Part I we cited the conclusions of other workers to the effect that nitration is of the second order, being of the first with respect both to the compound nitrated and to the nitrating agent. On account of the experiments described in Part IV, we doubt if the matter can in general be represented so simply. It is, however, unnecessary to assume such simplicity in order to derive our correction formula. The one essential assumption is that the *attack of the active nitrating entity* (whatever that may be) *on the aromatic compound is unimolecular with respect to the aromatic compound.* Nothing else matters: the active agent may be unknown and its attack may be of any total order; it may be produced in some preliminary change—

possibly slow, possibly reversible; it, or some material essential to it, may be simultaneously concerned in a dozen independent, or mutually interdependent, side reactions; all circumstances which would render hopeless any direct kinetic attack on the problem of relative rates of nitration: yet the competition method will give the right result. It will do so because, if the italicised assumption is fulfilled (as it almost certainly is) our logarithmic formula for $k_y/k_x$ is rigorous, and if it is not, we can still make $R$ as close an approximation as we please to $k_y/k_x$ by approaching the limit of small nitration. The one condition which *is* essential to the success of the competition method is that the reaction should be homogeneous. These matters are more fully illustrated in Part V, which describes a detailed kinetic investigation of nitration. The point to be made now is simply that the competition, not the kinetic, method is the correct one for solving the problem we are concerned to solve.

*Methods.*—Ethyl benzoate is only rather slowly nitrated, and therefore we used what, so far as we knew, was the most active nitrating agent that would give the necessary homogeneous solution, *viz.*, acetyl nitrate, prepared by mixing nitric acid and excess of acetic anhydride. With this reagent in excess, ethyl benzoate was considerably, though incompletely, mononitrated in, *e.g.*, 24 hours at room temperature (product analysed). Aromatic acid products were not formed in appreciable amount, a point of significance in relation to the methods of analysis. Benzene was rather easily nitrated with the same reagent, and little if any acid products were formed.

The task of analysing the mixture of nitrobenzene and ethyl nitrobenzoates arising in the competitive nitration of benzene and ethyl benzoate has presented unusual difficulty, essentially on account of the large difference in the speeds of the simultaneous reactions. The amount of ethyl nitrobenzoates formed was of the order of 1/200th of the amount of nitrobenzene; and for reasons already indicated the quantity of the latter was kept rather small in comparison with the excesses of initial materials. Thus the most difficult part of our task was to estimate a material constituting not much more than 1/2000th of the final mixture of aromatic compounds, and to do this with accuracy of a few units per cent. The result has been that minor side reactions and other disturbances, which would have been small enough to pass unnoticed had the proportions of materials been more normal, have in our case assumed such importance that each in turn had to be tracked down and eliminated. The interest of the chemistry involved is independent of the main subject of the paper, but this chemistry has been largely elucidated by survey of preliminary results and is inextricably concerned in the elaboration of method. Therefore we report these matters collectively in the following section in small type, and afterwards give in ordinary type a summary of those results which are of importance for the subsequent discussion.

*Analysis.*—In outline, the method of analysis was to digest the mixture with sodium hydroxide, and separate the neutral benzene and nitrobenzene from the hydrolytically-formed benzoic and nitrobenzoic acids by means of ether and alkali; then to estimate the nitrobenzene by a combination of distillation and reduction, and the nitrobenzoic acids by reduction (subsequent bromination was also considered).

The hydrolysis was checked by using purified ethyl benzoate and ethyl *o*-nitrobenzoate. Either ester was found to be hydrolysed practically completely after treatment at 100° for 20—23 hours with twice the calculated quantity of N-aqueous sodium hydroxide; but the addition of benzene and nitrobenzene decreased the rate of the hydrolysis, which could, however, be completed in 28 hours. No resinification or other noticeable change occurred when nitrobenzene alone was placed under these conditions, and there was no perceptible disappearance of alkali. The figures are not here reproduced, but the above statements can be attested with the accuracy to which titres of 20 c.c. can be read.

Nitrobenzene, in quantities of about 5 g., could not be estimated in mixtures with benzene, solely by distillation through Dufton columns, with an accuracy better than 2—3%; but by the use of such columns it was possible to remove most of the benzene without any detectable loss of nitrobenzene. The residue could then be weighed and portions taken for the estimation of nitrobenzene by reduction, a process which gains in convenience from the preliminary distillation.

Difficulty was experienced in the estimation by published methods of nitrobenzene by reduction with titanous chloride: probably owing to the volatility of nitrobenzene and its limited

solubility in aqueous solvents, low results, about 98%, were usually obtained. Therefore the following method was evolved. Alcohol (50 c.c.) was boiled (500 c.c. flask) under reflux for 5 mins. in a slow stream of carbon dioxide, which was greatly increased during the subsequent cooling by means of ice-water, and then reduced to 2 bubbles per sec., whereupon a small tube containing the weighed nitrobenzene together with a little benzene was introduced. A known excess of 0·25N-titanous chloride was added, and the mixture gently boiled for 30 mins. It was cooled, treated with 20% potassium thiocyanate solution (10 c.c.), and titrated with standard ferric alum (0·1N). The stream of carbon dioxide was continued throughout the process, and, near the end-point, the sides of the flask were washed down with water that had been boiled till free from air and cooled in carbon dioxide. This experiment was immediately followed by a "blank," in which the whole of the above procedure was followed except, first, that the nitrobenzene was omitted from the small tube, and secondly, that the amount of titanous chloride was equal to the former excess, the balance of the volume of liquid being made up with boiled-out, carbon dioxide-saturated water. In 11 experiments with purified nitrobenzene the errors were all negative, and the mean error was 0·22%; whilst for 8 of the experiments the individual errors were not more than this.

Purified samples of *o*-, *m*-, and *p*-nitrobenzoic acids were reduced, sometimes in the presence of added benzoic acid, by the same method, except that water was used in place of alcohol. All the errors were negative, the mean for 11 experiments being 0·08%.

Francis and Hill (*J. Amer. Chem. Soc.*, 1924, **46**, 2498) have developed a technique for the quantitative bromination of aromatic amines by means of bromide–bromate solution, and Flürscheim and Holmes (J., 1928, 448) have shown that, on treatment by this method at 30° for a suitable time, *o*-, *m*-, and *p*-aminobenzoic acids all give tribromination products (with loss of the carboxyl group in two cases). With purified samples of the three aminobenzoic acids this method gave satisfactory results (errors negative, average error in 7 experiments 0·21%), but when combined with a previous reduction of nitro-acids the results were very poor. We could discover no conditions in which an excess of titanous chloride could be destroyed by treatment with air or oxygen in such a way that subsequently added bromide–bromate solution could be titrated with potassium iodide and thiosulphate to give a stable end-point. In 15 experiments with purified nitrobenzoic acids the errors of estimation on the basis of bromine uptake varied from + 8·0 to − 7·1%, the average of the magnitudes of the errors being 3·9%. It therefore appears that the Francis–Flürscheim method of estimating nitro-compounds has not yet been described in a form to give results of high accuracy.

These processes (excepting the bromination) were synthesised into a complete method for the estimation of nitrobenzene and nitrobenzoic acids in mixtures containing also excesses of ben-
zene and ethyl benzoate, and the method was used at this stage of development in order to obtain
nitro... estimate of the proportions in which the nitro-compounds would be formed in competitive
ethyl benzoa...
excess. In the ... of five nitrations (series A) was carried out as follows. Benzene (0·1 g.-mol.)
alent proportions. ...te (0·1 g.-mol.) were together dissolved in acetic anhydride; and absolute
found to have unde...distilled with concentrated sulphuric acid, was separately dissolved in a small
$k_y/k_x$, in the limit of ...dride at 0°. The acetyl nitrate solution was added at a controlled rate to
nitrated is not small in ...ed solution of the aromatic compounds at not much above the room
approximation to $k_y/k_x$, ... was continued for a further 2 hours, and the mixture, after being kept
compounds get out of equ...poured on ice (400 g.), and left overnight to secure decomposition of the
The formula we use for this p...lution, basified with sodium hydrogen carbonate, was extracted 12
ation is clearly $R = (y_0 - y)$... ether, the extract was washed with water, and the washings were
aromatic compounds and $x$ an... combined extracts being then dried with *calcium chloride*. The
...20 drops a *minute*) through a long Dufton column, and the residue
It is important to consider ...s sodium hydroxide (250 c.c.) for 48 hours under reflux.
because it cannot, of course, be...n the benzene and nitrobenzene were extracted with the
cited the conclusions of other w...revious ether extraction, and the dried extract was evaporated as
being of the first with respect bo...lumn. The concentrate was transferred to a smaller still with a
account of the experiments desc...ne was removed, and the nitrobenzene was estimated as already
represented so simply. It is, how...s solution was acidified with concentrated hydrochloric acid
derive our correction formula. T...re extracted with 50 c.c. of pure ether 14 times. The extract
*nitrating entity* (whatever that may...water, and the washings re-extracted 9 times with 30 c.c. of
*the aromatic compound*. Nothing...n the dried total extract by distillation through a tall column,
attack may be of any total order...ed from the last traces of ether by a short exposure to the
...ere then estimated by reduction as already described. The

results are in Table I. Expt. A, 3 shows that the acetyl nitrate is largely consumed in some process other than the nitration of the aromatic compounds.

TABLE I.

*Competitive Nitrations (Series A).*

(Benzene, 0·1 g.-mol. Ethyl benzoate, 0·1 g.-mol. Room temperature.)

| No. | Time (hours). | $HNO_3$. (g.-mol.). | $Ac_2O$ (total) (g.-mol.). | Products (g.-mols.). $Ph{\cdot}NO_2$. | Products (g.-mols.). $C_6H_4(NO_2){\cdot}CO_2Et$. | Ratio, $\frac{C_6H_4(NO_2){\cdot}CO_2Et}{Ph{\cdot}NO_2}$. |
|---|---|---|---|---|---|---|
| 1 | 22 | 0·05 | 0·40 | 0·0144 | 0·000137 | 0·0095 |
| 2 | 46 | ,, | 0·30 | 0·0243 | 0·000187 | 0·0077 |
| 3 | 840 | ,, | ,, | 0·0240 | 0·000447 | 0·018 |
| 4 | 42 | 0·10 | 0·20 | 0·0577 | 0·000408 | 0·0071 |
| 5 | 52 | ,, | ,, | 0·0588 | 0·000369 | 0·0063 |

On account of the results of Table I the analytical method was further tested with artificial mixtures of approximately the following composition : benzene, 0·05 mol.; ethyl benzoate, 0·10 mol.; nitrobenzene, 0·05 mol.; ethyl nitrobenzoates (mixtures of the three isomerides), 0·0003 mol. A series of 17 experiments showed that with mixtures of this type the nitrobenzene could be estimated to within 0·7% (errors negative), and the ethyl nitrobenzoates to within 3% (errors both positive and negative). In view of the very large differences in the concentrations of these materials, this degree of precision was considered satisfactory.

Two further experiments were carried out in order to extend the check on the method from the commencement of the analysis back to the conclusion of the nitration, the primary object being to test for any loss of ethyl nitrobenzoates by hydrolysis in the dilute acid solution in which the acetic anhydride is left to complete its decomposition. Artificial mixtures of the same type were prepared, and these, as well as the appropriate quantities of nitric acid and acetic anhydride, were added to ice; the whole mixture was then left, and subsequently worked up as in a competitive nitration. The results had the accuracy already stated.

Two additions to the analytical routine here outlined were made subsequently and are described in the next sub-section.

*Nitration.*—All sources of serious error having been confined by exclusion to the nitration itself, a second series of competitive nitrations was carried through in order further to study this process. In the course of these 34 experiments (Series B) several possible sources of error were investigated. The proportion of ethyl benzoate nitrated is so minute that a very small proportion of a rapidly nitrating impurity (*e.g.*, a nuclear homologue) would seriously affect the results. We tried (*a*) purifying commercial ethyl benzoate by fractionation alone, (*b*) purifying it by partial freezing, and subsequent distillation of the less fusible portion and (*c*) preparing it ourselves from benzoic acid, which was prepared by oxidation of gum-benzoin. The conclusion was reached that the ethyl benzoate prepared by all these methods had the same properties with respect to the reaction studied. In a similar way we compared benzene samples derived from various sources and purified by various methods. We also compared different nitric acid samples, which were examined with special reference to possible effects due to oxides of nitrogen; also we examined different samples of acetic anhydride. As a result, our standard methods of obtaining materials for all the later experiments were as follows: Commercial ethyl benzoate was distilled five times through a Lapworth fractionating column, head and tail fractions being discarded, and the material being dried with sodium sulphate after each distillation. Kahlbaum's thiophen-free benzene was purified by partial freezing, dried with sodium, and fractionated. Kahlbaum's halogen-free nitric acid was freshly distilled with concentrated sulphuric acid. The acetic anhydride was Hopkin and Williams's "A.R." The nitrations were carried out in the dark, and allowed to proceed for 48 hours at room temperature. These conditions, except the time and in a minor degree the temperature, were maintained also in all later series of competitive nitrations.

These matters being largely routine, we do not quote the results of all the competitive nitrations of series B, but only a sufficient number to illustrate the discovery of another much more important source of error. This was detected when it was found that the apparent ratio of the ethyl nitrobenzoates to the nitrobenzene formed increased with the initial proportion of acetic anhydride. This means that acetic anhydride is being converted into a nitro-compound, which, after decomposition of the excess of acetic anhydride with water, is non-acidic and is therefore extracted with the aromatic nitration products. During the hydrolysis with alkali, however,

this product becomes acidic, retains nitroxyl (power of reducing titanous chloride), and is thus estimated falsely as nitrobenzoic acids. The amount of this acidic nitro-compound (or rather, these compounds—for we shall show later that there are more than one) is of the order of 1/1000th of the acetic anhydride used, and thus is of the same order as quantities of nitrobenzoic acids requiring estimation.

TABLE II.

*Competitive Nitration. Series B (abridged).*

(Benzene, 0·1 g.-mol. Ethyl benzoate, 0·1 g.-mol. Nitric acid, 0·1 g.-mol. Time, 48 hours. Room temperature.)

| No. | $Ac_2O$ (g.-mol.). | Products (g.-mol.). $Ph·NO_2$. | $C_6H_4(NO_2)·CO_2Et$. | Ratio, $C_6H_4(NO_2)·CO_2Et/Ph·NO_2$. |
|---|---|---|---|---|
| 4 | 0·2 | 0·05877 | 0·000516 | 0·0088 |
| 20 | 0·4 | 0·04027 | 0·001162 | 0·0286 |
| 27 | 0·6 | 0·02893 | 0·001163 | 0·0402 |
| 28 | 0·8 | 0·02369 | 0·001008 | 0·0426 |
| 25* | 0·4 | 0·03400 | 0·000245 | 0·0072 |

* Nitration product extracted with sodium sulphite—see text.

Concurrently with this series of competitive nitrations, the formation and methods of removal of the unwanted by-products were investigated by experiments of several different types. The first consisted of a single " dummy nitration " (series A) in which the conditions of competitive nitration were copied with the exception that the benzene and ethyl benzoate were omitted from the nitration mixture, but added to the ethereal extract of the product in order to disturb the analytical routine as little as possible. The initial quantities were: nitric acid 0·075 g.-mol., acetic anhydride 0·475 g.-mol. The product which remained neutral after the alkaline hydrolysis contained no detectable nitroxyl, whereas the acid product contained 0·000263 g.-mol. of nitroxyl. This is of the order of the quantities of nitrobenzoic acids to be estimated in the competitive nitrations.

Secondly, the methods of removal of nitromethane were considered. Chattaway showed that tetranitromethane could be prepared from nitric acid and acetic anhydride (J., 1910, **97**, 2099), and hence tri- and di-nitromethane and nitromethane might be produced also from these initial materials. Tri- and di-nitromethane are sufficiently acidic to be eliminated when, after decomposition of the excess of acetic anhydride with water, the whole nitration product is extracted from an aqueous solution basified with sodium hydrogen carbonate. In order to eliminate nitromethane completely from an ethereal solntion it was found necessary to extract it with 0·1N-aqueous sodium hydroxide. Further control experiments showed that this did not cause appreciable hydrolysis of ethyl nitrobenzoates under the conditions used. Therefore in all subsequent competitive nitrations the following addition was made to the analytical procedure. The ethereal extract of the whole nitration product was rapidly shaken three times with 30 c.c. of 0·1N-aqueous sodium hydroxide. The alkaline aqueous solution was extracted four times with 30 c.c. of ether, and these combined extracts were washed with a little water and added to the main extract.

A third, and somewhat lengthy, set of experiments was directed to the elimination of tetranitromethane. This has at least one property of the detected by-product since, being neutral, it would be extracted with the whole non-acidic nitration product, but, on alkaline hydrolysis, would be converted into the acidic substance, nitroform. It was hoped that the nitroform might be removed from the acid nitration product by distillation in steam, but in two nitrations, with the benzene and ethyl benzoate omitted at first but added before the separation (dummy nitrations, series B), it was found that only 41—42% of the acid product from the alkaline hydrolysis could be removed by distillation in steam. This indicates what is later confirmed, *viz.*, that there are at least two by-products to be dealt with.

The following five reactions were investigated with respect to their possible use in removing tetranitromethane:

(1) $C(NO_2)_4 + 2NaOH \longrightarrow C(NO_2)_3Na + NaNO_3 + H_2O$

(2) $C(NO_2)_4 + 2NaHCO_3 \longrightarrow C(NO_2)_3Na + NaNO_3 + H_2O + 2CO_2$

(3) $C(NO_2)_4 + Na_2SO_3 + 2NaOH \longrightarrow C(NO_2)_3Na + Na_2SO_4 + NaNO_2 + H_2O$

(4) $C(NO_2)_4 + Na_2SO_3 + 2NaHCO_3 \longrightarrow C(NO_2)_3Na + Na_2SO_4 + NaNO_2 + H_2O + 2CO_2$

(5) $C(NO_2)_4 + 2K_4Fe(CN)_6 \longrightarrow C(NO_2)_3K + 2K_3Fe(CN)_6 + KNO_2$

The investigation of each reaction usually consisted of four parts:

(*a*) Tetranitromethane was prepared by Chattaway's method, and ethereal solutions of various concentrations were shaken for various times with an aqueous solution of the reagent under examination. The tetranitromethane remaining in the ether was estimated by reduction with titanous chloride.

(*b*) Dummy nitrations of the type already described were carried out (series C), and experiments similar to those under (*a*) were made with the ethereal solution of the non-acidic nitration product. The residual tetranitromethane was estimated either as such, or as nitroform after alkaline hydrolysis as in a competitive nitration.

(*c*) The tetranitromethane of expts. (*a*) was replaced by ethyl *m*-nitrobenzoate.

(*d*) Expt. (*c*) was repeated with nitrobenzene in place of ethyl *m*-nitrobenzoate.

Altogether 32 experiments were carried out, with results which may be summarised as follows:

(1) Sodium hydroxide appeared to reduce titranitromethane and hydrolyse ethyl *m*-nitrobenzoate at comparable speeds. Both reactions proceeded partially when ethereal solutions were shaken for several hours with N-aqueous sodium hydroxide.

(2) Sodium hydrogen carbonate reduces tetranitromethane much faster than it hydrolyses ethyl *m*-nitrobenzoate. But the former reaction is too slow for practical use, being incomplete after several days, whether the reagent is employed in the solid form or as a concentrated aqueous solution. The hydrolysis of ethyl *m*-nitrobenzoate under corresponding conditions was negligible.

(3) A solution of sodium sulphite and sodium hydroxide attacks tetranitromethane and ethyl *m*-nitrobenzoate at comparable rates.

(4) A solution of sodium sulphite and sodium hydrogen carbonate was found to be a satisfactory reagent. For instance, a solution of 0·001036 g.-mol. of tetranitromethane in ether (60 c.c.) was shaken for 6·5 hours with a solution of 0·01 g.-mol. of sodium sulphite and 0·003 g.-mol. of sodium hydrogen carbonate in water (25 c.c.): 99·7% of the tetranitromethane was extracted. When ethyl *m*-nitrobenzoate was used only 1·2% of it was hydrolysed. Nitrobenzene was unaffected. When the products of dummy nitrations were similarly examined, only about 50—60% of the nitroxyl could be extracted. This confirms the previous conclusion that part of the by-product, which appears ultimately as an acidic nitro-compound, is not tetranitromethane, although another part has the properties of tetranitromethane.

(5) Potassium ferrocyanide gives results quite similar to those obtained with sodium sulphite and sodium hydrogen carbonate. The usual method was to shake an ethereal solution (about 50 c.c.) of the material to be examined with a solution of the ferrocyanide (4 g.) in water (20 c.c.) for about 7 hours.

We thus had two reactions, *viz.*, (4) and (5), by which to remove tetranitromethane from our nitration products. They worked equally well, and both were used in the later competitive nitrations of series B; the application of method (4) is illustrated in Table II (expts. 25 and 20). Both were used also in the benzene nitrations of series A, in the ethyl benzoate nitrations (series A), as well as, of course, in the dummy nitrations of series C. By the time we came to do the measurements to which all this work was preparatory, *viz.*, the competitive nitrations of series C and the benzene nitrations of series B, we had, for no particular reason, formed the habit of using method (4), and we therefore give the exact technique of this second modification in the original analytical procedure.

The ethereal extract of the whole nitration product was concentrated as before by slow distillation through a Dufton column, but from a ground-jointed bottle instead of a flask; and then, instead of proceeding immediately with the hydrolysis, the distillation of ether was stopped before it was quite finished and the column was washed with ether back into the bottle. A solution of crystallised sodium sulphite (2·5 g.) and sodium hydrogen carbonate (0·3 g.) in water (25 c.c.) was then added, and the bottle was stoppered and shaken for 7·5 hours at room temperature. The faintly yellow ethereal layer was washed twice with 25 c.c. of water, once with 30 c.c. of 0·05N-aqueous sodium hydroxide, and again twice with 25 c.c. of water. The orange-red sulphite solution was extracted 6 times with 25 c.c. of ether, and the ether was washed once with 25 c.c. of water, once with the 30 c.c. of the aqueous sodium hydroxide used previously, and twice with water. The combined water washings were extracted 6 times with 30 c.c. of ether, and the extract was washed with the same sodium hydroxide solution and then with water. The last wash-water was combined with the sodium hydroxide solution and extracted 4 times with 25 c.c. of ether, the extract being washed with a little water. The ether was removed from the combined and dried ethereal extracts by slow distillation through a Dufton column, and the

residue was hydrolysed as before. This procedure ensures the removal of any trace of nitromethane that might be formed from tetranitromethane during the distillation or sulphite treatment; and of any nitrophenols that might have arisen by the action of sulphite on dinitrobenzenes.

A fourth set of experiments was carried out in order to discover how to deal with the second by-product arising from the nitration of the acetic anhydride. We still do not know what this is. It is non-acidic, and not reduced by sodium sulphite or potassium ferrocyanide; but it is converted by sodium hydroxide into an acidic, nitroxyl-containing substance, which is not volatile in steam (this is more definitely proved later). This last property suggested that the second by-product might be a rather complex substance, and might be formed, therefore, at a late stage of a long sequence of reactions. If so, it should be possible to minimise or eliminate the formation of the substance by cutting down the time of reaction; for by reducing the time we favour the products of earlier as against those of later stages of a series of consecutive reactions. Thi idea was worked out in a series of 8 benzene nitrations run for different times (series A). The conditions were substantially those of the competitive nitrations, except that the ethyl benzoate was left out of the nitration mixture, but added to the ethereal extract of the product before the separation in order to keep standard the conditions of analysis. The benzene was put in, and the nitrobenzene formed was measured, in order to show the time-variation of an initial process typical of the two rates we want to compare. The ethyl benzoate was left out of the nitration since the object was to discover conditions in which no nitro-acids were produced which would be estimated incorrectly as nitrobenzoic acids. The nature of the time effect is shown in Table III, in which we have included only experiments run for the longest and shortest times investigated; the other experiments gave consistent intermediate values. It will be observed that when the time is reduced from 48 to 9 hours the amount of nitrobenzene drops very little. The tetranitromethane, which must be the product of several consecutive reactions, is reduced much more, though not nearly enough to allow us to abandon the process already worked out for removing it. In contrast, the second by-product is reduced to almost a negligible quantity.

TABLE III.

*Benzene Nitrations. Series A (abridged).*

(Benzene, 0·1 g.-mol. Nitric acid, 0·1 g.-mol. Acetic anhydride, 0·4 g.-mol. Room temperature. In some experiments sulphite–bicarbonate was used to extract tetranitromethane, and in others ferrocyanide, the two reagents being equally effective.)

| | Time | Products (g.-mol. × $10^{-5}$). | | |
|---|---|---|---|---|
| No. | (hours). | Nitrobenzene. | Tetranitromethane. | 2nd By-product. |
| 3 | 48 | 5511 | 66·9 | 44·8 |
| 8 | 9 | 5079 | 23·2 | 4·2 |

The fifth group of experiments consisted in a short series (A) of ethyl benzoate nitrations, with benzene omitted from the nitration but added before the separation of products. The results, not quoted in detail, show that, in nitration for 9 hours at room temperature the amount of ethyl nitrobenzoates formed from 0·1 g.-mol. of ethyl benzoate, the quantities of nitric acid and acetic anhydride being as stated in Table IV, is about 40 × $10^{-5}$ g.-mol., *i.e.*, approximately ten times the quantity of the second by-product. This means that, in a competitive nitration under corresponding conditions, the error in the estimation of ethyl nitrobenzoates, due to the second by-product, would be of the order of 10%. However, this error can obviously be reduced by shortening the time still further, or, alternatively by reducing the temperature.

To complete our preparations for the measurements of relative nitration rates, we examined the possibility of the formation of a by-product from benzene, *viz.*, *o*-dinitrobenzene, which up to the present might not have been distinguished from the second by-product from acetic anhydride. *o*-Dinitrobenzene will be produced in appreciable quantity if there is any significant amount of dinitration of benzene. Being non-acidic it would accompany the neutral nitration product; it might not be reduced by sulphite or ferrocyanide, but it might be hydrolysed by alkali to *o*-nitrophenol, which, as a nitroxyl-containing acid, would be estimated with the nitrobenzoic acids. A direct comparison was therefore made between the volatility in steam of *o*-nitrophenol and of the second by-product (free from nitroform) derived from one of the benzene nitrations, distillates and residues being tested for nitroxyl as usual by reduction with titanous chloride. It was found that, under conditions in which *o*-nitrophenol is practically completely distilled, the second by-product remains almost wholly in the undistilled material. The second by-product cannot therefore contain any appreciable quantity of *o*-nitrophenol

In the final series of competitive nitrations the reaction time was diminished to 6 hours, and the temperature was also reduced. The previous nitrations had been done at, or slightly above, 20°; but now the standard temperature was taken as 18°, the upper limit during admixture of the reagents being 18·5°. By these means we expected to make the error due to the second by-product of the same order as the error of analysis.

*Results.*—The reagents used in the competitive nitrations were taken in the following quantities: benzene 0·1 g.-mol., ethyl benzoate 0·1 g.-mol., nitric acid 0·1 g.-mol., and acetic anhydride 0·4 g.-mol. The nitric acid was mixed at 0° with 0·1 g.-mol. of acetic anhydride, and the aromatic compounds were mixed at 18° with the remaining 0·3 g.-mol. of the acetic anhydride. The addition of the nitrating solution to the other materials occupied about 20 minutes. Mechanical stirring was employed. The mixture was kept at 18° for 6 hours, counting from the mean time of addition of the nitrating solution, and then poured on ice. The nitration products were separated and estimated as already described.

The quantities of nitrobenzene and of ethyl nitrobenzoates produced are given in Table IV. The estimates of ethyl nitrobenzoates are rendered a little too high owing to incomplete elimination of the "second by-product." The order of magnitude of this error is elucidated later. The indicated uncertainty in the mean of the uncorrected ratios $R$ is the probable error calculated by the usual formula.

TABLE IV.

*Competitive Nitrations (Series C).*

| No. | Products (g.-mols. × $10^{-5}$). Nitrobenzene. | Ethyl nitrobenzoates. | Ratio, $R$ = $C_6H_4(NO_2)\cdot CO_2Et/Ph\cdot NO_2$. |
|---|---|---|---|
| 1 | 3219 | 14·4 | 0·00447 |
| 2 | 3040 | 16·0 | 0·00526 |
| 3 | 3195 | 14·4 | 0·00451 |
| 4 | 3037 | 13·7 | 0·00451 |
| 5 | 3434 | 13·8 | 0·00402 |
| 6 | 3412 | 16·8 | 0·00492 |
| 7 | 2948 | 13·1 | 0·00444 |
| 8 | 2798 | 12·4 | 0·00442 |

Mean $R$ (uncorrected) = 0·00457 ± 0·00009.

In order to provide a "blank" for the difficult part of these analysis, *viz.*, the estimation of ethyl nitrobenzoates, a short series of benzene nitrations was subsequently carried out (Series B). The experimental conditions were the same as for the mixed nitrations, except that the ethyl benzoate was left out of the nitration mixture but was added to the nitration product before separation in order not to disturb the analytical routine. The results are in Table V. The second by-prodnct is the material which would have been estimated as ethyl nitrobenzoates in a competitive nitration.

TABLE V.

*Benzene Nitrations (Series B).*

| No. | Products (g.-mols. × $10^{-5}$). Nitrobenzene. | Tetranitromethane. | 2nd By-product. |
|---|---|---|---|
| 1 | 3929 | 12·1 | 1·5 |
| 2 | 4301 | 12·8 | 0·9 |
| 3 | 4195 | 11·5 | 1·4 |
| 4 | 4007 | 12·0 | 1·1 |

(2nd By-product: Mean = 1·2 × $10^{-5}$ g.-mol.)

Since the figures in the fourth column of this table are above the magnitude of the analytical error (± 0·4 × $10^{-5}$ g.-mol.), it is clear that finite amounts of the second by-product must be formed in these nitrations, and therefore in the competitive nitrations, but it is not easy to compute the correction to be applied to the estimates of ethyl nitrobenzoates in Table IV. An upper limit to the magnitude of the correction can be given, because we have shown (section in small type) that when, as by a reduction in the time, the reaction

is confined to a more initial period, the quantity of second by-product is reduced in greater proportion than is the quantity of nitrobenzene. Taking average figures from Tables IV and V we find that the dilution effect of the (chemically rather unreactive) ethyl benzoate additionally present in the competitive nitrations reduces the amount of nitrobenzene formed from 4108 to 3135 $\times$ $10^{-5}$ g.-mol., *i.e.*, by the factor 0·76. Therefore the quantity of second by-product must have been reduced from 1·2 $\times 10^{-5}$ to something less than 0·9 $\times 10^{-5}$ g.-mol. The negative correction to be applied to the estimates of ethyl nitrobenzoate lies therefore between 0·9 $\times$ $10^{-5}$ g.-mol. and zero, and arbitrarily we take the mean, 0·5 $\times$ $10^{-5}$ g.-mol. Recalculating the values of the ratio $R$ from these corrected estimates we find 0·00441 $\pm$ 0·00015. Here the indicated error covers the whole range of uncertainty in the correction. Assuming that all corrections within this range have equal probability, we can calculate an over-all probable error and thus obtain :

$$\text{Mean } R \text{ (corrected)} = 0{\cdot}00441 \pm 0{\cdot}00010.$$

We have still to calculate $k_y/k_x$, which is appreciably different from $R$, owing to the fact that the benzene underwent as much as 31% of the possible amount of nitration, so that the original equivalence of the benzene and ethyl benzoate concentrations was not maintained throughout the reaction. We find :

$$k_y/k_x = 0{\cdot}00367 \pm 0{\cdot}00008.$$

In other words, the specific rate of nitration of ethyl benzoate is 272 $\pm$ 6 times smaller than that of benzene under the conditions used.

### (2) *Proportions of Isomerides Formed in the Nitration of Ethyl Benzoate with Acetyl Nitrate in Acetic Anhydride at* 18°.

The proportions in which *o*-, *m*-, and *p*-nitro-derivatives are formed when ethyl benzoate is nitrated with nitric acid at $-$ 40°, at 0°, and at 30° have been determined by Holleman (*Z. physikal. Chem.*, 1899, **31**, 79). We have carried out the same determination for nitration with acetyl nitrate in acetic anhydride at 18°, the reagent and temperature employed in the competitive nitrations. We had to use, however, a more concentrated solution of acetyl nitrate in acetic anhydride, and also a larger proportion of acetyl nitrate relatively to ethyl benzoate, than in the competition experiments, in order to obtain sufficient nitro-esters for the estimation of the separate isomerides. The mixed nitro-esters were hydrolysed to nitro-acids, in which the *o*-, *m*, and *p*-isomerides were estimated by a modification of Holleman's leaching-out method.

*Analysis.*—In the leaching-out method, an acid is estimated in admixtures with other acids by the increase in acidity which it brings about in a solution previously saturated with respect to all the other acids. Thus *o*-nitrobenzoic acid is leached out from a mixture of the three isomerides by means of a solution saturated with the *m*- and the *p*-acid. In this process any non-isomeric, acid impurities would also be leached out and estimated as *o*-nitrobenzoic acid ; wherefore the original method is extended by separately leaching out, and estimating, the non-isomeric acids by the use of a solution saturated with the *o*-, *m*-, and *p*-nitro-acids (Baker and Ingold, J., 1927, 569).

It was arranged to use sufficient water to leach out the whole of each of the acids to be estimated in one step (Holleman conducted successive leachings). The leachings were carried out at 25·0°, and each leaching solution was made with 150 c.c. of water and the stated quantities (more than enough to secure saturation) of two, or of all three, of the nitro-acids : ortho- 2 g., meta- 1 g., para- 0·1 g. The quantities of mixed acids used for the determinations of the *o*-, *m*-, and *p*-nitro-acids, and of the non-isomeric acids, were respectively about 1 g., 0·5 g., 0·8 g., and 0·5 g.

Each determination required two flasks, each fitted with a mercury-sealed stirrer and immersed to the neck in the thermostat. Each flask was charged with 150 c.c. of water, and with the nitro-acids with which the leaching solution was to be saturated ; and to one flask was added a weighed quantity of the mixed acids requiring analysis. The flasks were stirred for not less than 20 hours, and a sample was withdrawn from each by means of a pipette fitted with a detachable filter tube, which was allowed to come into adsorption equilibrium with the solution before passage of the sample. The samples were titrated with 0·05N-barium hydroxide,

phenolphthalein being the indicator; the difference of titre measured the increase of acidity due to the leached out acid. After further periods of stirring, further samples were similarly withdrawn and titrated in order to check the completeness of the leaching.

The increase of acidity due to the addition of a nitrobenzoic acid to a saturated solution of its two isomerides is in general not exactly equivalent to the added acid, because the dissolution of this acid causes a change in the solubility of the isomerides with which the solution remains saturated. It is therefore necessary empirically to determine the correction which will convert observed increases of acidity into weights of leached out acid. For the sparingly soluble *p*-nitro-acid, over the required range, the correction is negligible. For the more soluble *o*- and *m*-acids, it is not: it appears that the addition of *o*-acid to a solution saturated with respect to the *m*- and *p*-acids throws the *m*-acid out of solution, whilst the addition of *m*-acid to a saturated solution of the *o*- and *p*-acids causes more *o*-acid to dissolve. The following data were determined, and used to construct correction curves:

*o*-Nitrobenzoic acid (added to 150 c.c. of water containing dissolved and suspended *m*- and *p*-nitrobenzoic acids, at 25°; weights in mg.):

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *Added* | 126·4 | 143·1 | 197·9 | 200·8 | 220·8 | 237·6 | 244·4 | 300·5 |
| Found | 101·4 | 118·3 | 166·2 | 169·9 | 191·3 | 209·5 | 215·1 | 268·8 |
| Corr. | +25·0 | 24·8 | 31·7 | 30·9 | 28·5 | 28·1 | 29·3 | 31·7 |

*m*-Nitrobenzoic acid (added to 150 c.c. of water containing dissolved and suspended *o*- and *p*-nitrobenzoic acids, at 25°; weights in mg.):

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Added | 246·8 | 287·9 | 322·8 | 326·3 | 347·4 | 369·0 | 398·8 |
| Found | 267·8 | 315·3 | 350·9 | 357·8 | 376·1 | 411·7 | 450·9 |
| Corr. | −20·8 | 27·4 | 28·1 | 31·5 | 28·7 | 42·7 | 52·1 |

*Nitration.*—Materials were obtained and purified as for the final series of competitive nitrations.

Ethyl benzoate (0·15 g.-mol.) was mixed with acetic anhydride (0·1 g.-mol.). Nitric acid (0·75 g.-mol.) was mixed with acetic anhydride (0·75 g.-mol.) at 0°, and this solution was added with mechanical stirring to the ester solution at 18·0—18·5°. The mixture was kept at 18° for 8 hours, and poured on ice. After the acetic anhydride had decomposed, the solution was basified with sodium hydrogen carbonate and extracted with ether. The extract was washed with sodium hydroxide and water, dried, and evaporated. The tetranitromethane and a good deal of ethyl benzoate were removed by distillation from a boiling water-bath, at pressures reduced finally to 1 mm. By using a glycerol-bath, the ethyl nitrobenzoates were collected at 1 mm. pressure and at bath-temperatures between 100° and 170°; they distilled mainly at 128°/1 mm.

The nitro-esters were saponified for 24 hours at 100° with twice the theoretical amount of N-aqueous sodium hydroxide; and, after acidification with hydrochloric acid, the nitro-acids were isolated by extraction with ether.

The nitro-acids contained a good deal of benzoic acid, most of which was removed by distillation in steam, though with some loss of nitro-acids. The distillations were controlled by titration of successive portions of the distillate first with barium hydroxide, and secondly with titanous chloride. Under the conditions used, the removal of most of the benzoic acid involved a loss of about 4% of nitro-acids. The distribution of this loss amongst the three isomerides was computed on the basis of measurements of the rates at which the three nitro-benzoic acids distil in steam when introduced into the still in the quantities in which they would be present in the purification of a nitration product. Thus a 4·0% loss was found to be distributed as follows: ortho- 0·9; meta- 2·1; para- 1·0%.

The nitro-acids recovered by ether extraction from the residue of the distillation in steam contained non-volatile impurities, which were largely removed by sublimation. The specimen was placed in a boiling tube, into which a somewhat shorter and narrower water-cooled tube was fitted. The outer tube was immersed in a bath at 130°, whilst the pressure in the annular space was reduced to 0·04 mm. In this apparatus an artificial mixture of mononitrobenzoic acids distilled completely to form a firm cake on the inner tube, from which it could readily be detached. When applying this method to the mixed nitro-acids recovered from the steam-distillation, the heating bath was carried up to 160°. A little tar remained in the outer tube. The distilled acids, which had a very pale cream colour, were detached from the inner tube, and ground for analysis. They still contained acidic impurities, which were dealt with in the estimation process as already described.

*Results.*—We first record the detailed results of a typical analysis (nitration IV, analysis 2) :

*Non-nitrobenzoic acids.* Mixed acids taken for analysis, 0·5187 g. Leaching solution, 150 c.c. of water with dissolved and suspended *o*-, *m*- and *p*-nitro-acids. Samples of 25 or 50 c.c. were withdrawn, but titres are given below as for 50 c.c. samples. Barium hydroxide solution, N/19·95.

| | | | | |
|---|---|---|---|---|
| Time stirred (hours) | 21 | 25 | 40 | 48 |
| Analysis titre (c.c.) | 69·56 | 69·48 | 69·52 | 69·67 |
| Control titre (c.c.) | 68·15 | 68·07 | 68·09 | 68·43 |
| Difference (c.c.) | 1·41 | 1·41 | 1·43 | 1·24 |

Mean difference, 1·38 c.c. Barium hydroxide equivalent to non-nitrobenzoic acids per g. of sample, 7·93 c.c. (Calculated as benzoic acid this is equivalent to 4·9% by weight. All other nitration products had smaller proportions of non-nitro-benzoic acids, the smallest being 2·8%, calculated as benzoic acid.)

o-*Nitrobenzoic acid.* Mixed acids taken, 1·0048 g. Leaching solution, 150 c.c. of water with dissolved and suspended *m*- and *p*-nitro-acids. Titres given as for 50 c.c. samples. Barium hydroxide, N/19·95.

| | | | |
|---|---|---|---|
| Time stirred (hours) | 21 | 25 | 39 |
| Analysis titre (c.c.) | 32·64 | 32·67 | 32·61 |
| Control titre (c.c.) | 22·07 | 22·21 | 22·26 |
| Difference (c.c.) | 10·57 | 10·46 | 10·35 |

Mean difference, 10·46 c.c. Excess acidity due to the whole analysis sample, 31·38 c.c. Excess acidity due to *o*-nitrobenzoic acid, 23·41 c.c. Corresponding weight of nitrobenzoic acid, 0·1960 g. Correction for changes of solubility, + 0·0285 g. Weight of *o*-nitrobenzoic acid, 0·2245 g. = 22·3% of sample.

m-*Nitrobenzoic acid.* Mixed acids taken, 0·5040 g. Leaching solution, 150 c.c. of water with dissolved and suspended *o*- and *p*-nitro-acids. Titres as for 50 c.c. samples. Barium hydroxide, N/19·95.

| | | | |
|---|---|---|---|
| Time stirred (hours) | 20 | 26 | 28 |
| Analysis titre (c.c.) | 60·85 | 60·58 | 60·77 |
| Control titre (c.c.) | 44·54 | 44·45 | 44·48 |
| Difference (c.c.) | 16·31 | 16·13 | 16·29 |

Mean difference, 16·24 c.c. Excess acidity due to whole analysis sample, 48·72 c.c. Excess acidity due to *m*-nitrobenzoic acid, 44·72 c.c. Corresponding weight of nitrobenzoic acid, 0·3743 g. Correction for changes of solubility, — 0·0289 g. Weight of *m*-nitro-acids, 0·3454 g. = 68·5% of sample.

p-*Nitrobenzoic acid.* Mixed acids taken, 0·6072 g. Leaching solution, 150 c.c. of water with dissolved and suspended *o*- and *m*-nitro-acids. Titres as for 50 c.c. samples. Barium hydroxide, N/19·95.

| | | | |
|---|---|---|---|
| Time stirred (hours) | 21 | 39 | 40 |
| Analysis titre (c.c.) | 69·36 | 70·15 | 69·36 |
| Control titre (c.c.) | 66·88 | 67·65 | 66·95 |
| Difference (c.c.) | 2·48 | 2·50 | 2·41 |

Mean difference 2·46 c.c. Excess acidity due to whole analysis sample, 7·38 c.c. Excess acidity due to *p*-nitrobenzoic acid, 2·57 c.c. Weight of *p*-nitrobenzoic acid, 0·0212 g. = 3·5% of sample.

*Correction of percentages.* Corrections to the given percentages by weight of the sample are necessary on account of impurities in, and losses from, the sample. The observed percentages by weight of *o*-, *m*-, and *p*-nitrobenzoic acids in the sample total 94·3%, and the remaining 5·7% is attributed to non-nitrobenzoic acids present as impurities. The percentages by weight of *o*-, *m*-, and *p*-nitrobenzoic acids, not in the sample itself, but in the total nitrobenzoic acids in the sample, are therefore : ortho- 23·5, meta- 72·8, para- 3·7%. The purification losses of the three nitrobenzoic acids, determined as described in the section in small type, are : ortho- 0·9, meta- 2·2, para- 1·0% by weight of the nitrobenzoic acids in

the purified sample. Therefore the percentages of the isomerides, calculated in the total mononitro-compounds formed in the nitration, are: ortho- 23·4, meta- 72·1, para- 4·5%.

In all, five nitrations were carried out; but the first two were done before the technique of purification and analysis was fully elaborated, and the results were therefore unreliable. The last three nitrations gave material for five independent analyses, the results of which are in Table VI. The meaning of the three sets of percentages will be clear from the preceding paragraph.

TABLE VI.

*Nitrations of Ethyl Benzoate.*

Percentages of *o*-, *m*-, and *p*-isomerides.

| Expt. No. | In sample. | | | | In isomerides in sample. | | | In isomerides formed. | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Non-. | Ortho-. | Meta-. | Para-. | Ortho-. | Meta-. | Para-. | Ortho-. | Meta-. | Para- |
| III | 5·8 | 22·7 | 68·2 | 3·3 | 24·1 | 72·4 | 3·5 | 24·0 | 71·7 | 4·3 |
| IV 1 | 3·2 | 23·8 | 69·9 | 3·1 | 24·6 | 72·2 | 3·2 | 24·5 | 71·5 | 4·0 |
| IV 2 | 5·7 | 22·3 | 68·5 | 3·5 | 23·5 | 72·8 | 3·7 | 23·4 | 72·1 | 4·5 |
| V 1 | 3·4 | 23·4 | 70·7 | 2·5 | 24·2 | 73·2 | 2·6 | 24·1 | 72·4 | 3·5 |
| V 2 | 3·1 | 23·8 | 70·6 | 2·5 | 24·5 | 72·9 | 2·6 | 24·4 | 72·1 | 3·5 |

The final mean values for, and formal probable errors in, the percentages in which the three mononitro-isomerides are formed in the nitration of ethyl benzoate with acetyl nitrate in acetic anhydride at 18° are therefore as follows:

ortho-, 24·1 ± 0·1%; meta-, 72·0 ± 0·1%; para-, 4·0 ± 0·1%.

(3) *Partial Rate Factors for the Nitration of Ethyl Benzoate by Means of Acetyl Nitrate at* 18°.

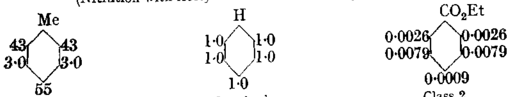
By combining the results of the sections (1) and (2) we can calculate the partial rate factors for the nitration of ethyl benzoate under the conditions used. A partial rate factor is defined as the factor by which the replacement of a hydrogen atom in benzene by an orienting substituent, in our case carbethoxyl, alters the probability of substitution at an individual nuclear carbon atom (if there are several equivalent atoms we suppose them labelled).

The probability of snbstitution at a particular carbon atom in benzene is taken as equal to unity. The probability for the whole benzene molecule is thus 6. The probability for the whole ethyl benzoate molecule is therefore 6 × 0·00367 = 0·0220, from the rate data. From the orientation data it follows that this probability is distributed amongst the five available positions, taken in order round the ring, in proportion to the factors 24·1/2, 72·0/2, 4·0, 72·0/2 and 24·1/2%.

Thus the partial rate factors for ethyl benzoate are as shown in the third of the following formulæ. The partial rate factors for toluene, for the same nitrating agent and interpolated to the same temperature from the results of Part II, are given for comparison.

*Effect of* Me *and* $CO_2Et$ *on Probability of Substitution.*

(Nitration with Acetyl Nitrate in Acetic Anhydride at 18°.)




Class 1. Standard. Class 2.

Just as the methyl substituent (Class 1) activates all positions, but the *o*- and *p*-positions more than the *m*-, so the carbethoxyl group (Class 2) deactivates all positions, the *o*- and *p*- more than the *m*-.

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# 176. *Influence of Directing Groups on Nuclear Reactivity in Oriented Aromatic Substitutions. Part IV. Nitration of the Halogenobenzenes.*

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The investigation of the effect of single substituents in benzene on the rate of nitration at each nuclear position, commenced with the examples toluene (Part II) and ethyl benzoate (Part III), is here continued with the four halogenobenzenes, two of which are investigated accurately and two with less precision. The main part of the work consists in determining the rate of nitration of these substances in terms of the rate of nitration of benzene. Experiments have also been carried out on the orientation of nitration. The rates of total nitration by acetyl nitrate in acetic anhydride at 18° are ($C_6H_6$ = 1): $C_6H_5F$, 0·15; $C_6H_5Cl$, 0·033; $C_6H_5Br$, 0·030; $C_6H_5I$, 0·18. Thus the halogenobenzenes are *op*-orienting by differential deactivation, unlike toluene, which is also *op*-orienting but by differential activation; and also unlike ethyl benzoate, which is *m*-orienting by the opposite kind of differential deactivation. The circumstance that the rates of nuclear nitration pass through a minimum in the halogen series contrasts with the monotonic variation of rates, *i.e.*, the absence of an intermediate minimum or maximum, which in general is observed when nuclear halogens affect reactions in aromatic side chains. The difference is attributed to the greater relative importance of polarisability effects, particularly the electromeric effect, in nuclear than in side-chain substitution; and it is deduced that these effects collectively are electron-releasing in the order I > Br > Cl > F.

In the examples of chloro- and bromo-benzenes the effect of conditions has been investigated, three solvents and three temperatures being employed. The solvent effect on the relative reaction rates is small and irregular, but the temperature effect is rather large and regular. It is such as to show that the orienting substituents change the rates of reaction at the several nuclear positions mainly by changing the energies, rather than the entropies, of activation.

THIS paper continues the investigation of the effects of single substituents in benzene on the rate of nitration in the various nuclear positions. The general theory was given in Part I (J., 1927, 2918), where substituents were shown to fall into four classes. Parts II and III (J., 1931, 1959, and preceding paper) having dealt with toluene and ethyl benzoate in exemplification of classes 1 and 2, we are now concerned with the halogenobenzenes which illustrate class 3. As before, our object is to determine the factors by which the original substituent alters the probability of substitution at each nuclear position; and the principal measurement involved is that of the rate of nitration of the substituted benzene in terms of the rate of nitration of benzene. Some preliminary experiments on the halogenobenzenes were recorded in Part I, but the analytical methods were at that time insufficiently studied to give quantitative value to the results.* We have now examined chloro- and bromobenzene rather accurately, fluorobenzene less exactly, and iodobenzene in outline.

In the work on toluene, it was attempted to investigate the influence of change in the nitration medium and the temperature on the factors expressing the effect of the substituent on the rate of substitution; but the variations were small, and the demonstration of them was only partly successful. In the case of ethyl benzoate the analytical procedure was so lengthy that attention was concentrated on establishing values for a single set of conditions. Having available in the examples of chloro- and bromo-benzene a fairly accurate analytical method, we returned to the problem of the influence of conditions; and we are able now to show that the effect of temperature approximately follows a simply interpretable law.

### (1) *Relative Rates of Nitration of Chlorobenzene, Bromobenzene, and Benzene by Means of Acetyl Nitrate in Acetic Anhydride, Acetonitrile, or Nitromethane at 0°, 25°, and 35°.*

We have again employed the competition method, which, as pointed out in previous parts, is the correct method for the solution of this problem. It will be recalled that the

* The qualitative result of Part I for iodobenzene, *viz.*, that it is nitrated faster than benzene, was reproduced by us on a single occasion (Expt. 81), but we cannot confirm it at will, and think that it must be in error through some disturbance not yet elucidated (cf. p. 926).

ratio, $R$, in which the halogenobenzene and benzene are found to have undergone nitration, tends to the ratio, $k_y/k_x$, of their specific rates of nitration in the limit of small amounts of reaction; and otherwise, $R$ can be corrected accurately to give $k_y/k_x$.

*Analysis.*—The problem is the analysis of a mixture of benzene, halogenobenzene, nitrobenzene, and halogenonitrobenzenes, and, in particular, the estimation of the last two constituents, present to the extent of perhaps 5% and 0·2% respectively, each with an accuracy of 1 or 2 units %. The halogenonitrobenzenes consisted practically exclusively of the *o*- and *p*-isomerides, and hence the method was to estimate the total nitro-compounds by reduction with titanous chloride, and then to estimate the halogenonitrobenzenes by alcoholysis with sodium methoxide.

For the measurement of total nitro-compounds, Sempey's stannous chloride method (*J. Amer. Chem. Soc.*, 1930, **52**, 88) was tried and found to give inaccurate results. The titanous chloride method (preceding paper) was checked with nitrobenzene, *o*- and *p*-chloro-, and *o*- and *p*-bromo-nitrobenzene and gave values 0·1—0·3% (rarely 0·5%) low—a result which was considered satisfactory.

For the estimation of halogenonitro-compounds the sodium methoxide method, used in similar work by Ingold and Vass (J., 1928, 423), was found to give good results provided the methyl alcohol was carefully dehydrated with magnesium. Our practice was to heat as much of the mixture to be analysed as would contain about 0·001 g.-mol. of halogenonitro-compound with sodium methoxide solution, prepared from 5 g. of sodium and 100 c.c. of methyl alcohol, for 24 hours at 100° under reflux, then to distil off the methyl alcohol with additions of water, and finally to acidify the solution with nitric acid and estimate halide ion. In 10 tests on mixtures comparable in composition to the competitive nitration products the errors in the estimation of halogenonitro-compounds were all negative and averaged 0·5%. The halide ion was at first estimated by Volhard's method, but this was later replaced by the electrometric method of Müller and Cavanagh, with increase in convenience and accuracy.

*Nitration.*—Materials were purified as follows. Kahlbaum's pure nitric acid was distilled from concentrated sulphuric acid in an all-glass still; it was sometimes freshly vacuum-distilled to remove nitrous acid. Acetic anhydride, acetonitrile, and nitromethane were dried and fractionated. Thiophen-free benzene was fractionally frozen, with subsequent drying and distillation, until the f. p. was constant and correct. Chloro- and bromo-benzene were also fractionally frozen, dried, and fractionally distilled several times.

The nitration of chloro- and bromo-benzene in mixtures of nitric acid and acetic anhydride, diluted with excess of acetic anhydride, acetonitrile, or nitromethane, was first examined with respect to the products. These consisted of unchanged material and mononitro-derivatives, but no dinitro-compounds, since the last fraction obtained on distillation had the correct nitroxyl content for mononitro-compounds. An attempt further to nitrate an artificial mixture of *o*- and *p*-bromonitrobenzene with acetyl nitrate in acetic anhydride led only to a very small increase in nitroxyl content. "Dummy" nitrations were carried out in order to control the possibility of error in the estimation of aromatic nitro-compounds due to the formation of tetranitromethane or any other product of nitration of the solvent. It was shown that under the conditions of the competitive nitration such errors could not amount to more than 0·5%, and would normally be considerably less, and therefore in any case would be within the analytical error.

The general method of nitration was as follows. A mixture of nitric acid (0·0375 g.-mol.) and acetic anhydride (0·0375 g.-mol.) diluted with the solvent (excess of acetic anhydride, acetonitrile, or nitromethane, usually 6 c.c.), was made at 0°. This was added with mechanical stirring to a solution of benzene (0·0500 g.-mol.) and halogenobenzene (0·0500 g.-mol.) in the solvent (usually 20 c.c.) at the required temperature (0°, 25°, or 35°), and the mixture was kept at this temperature for the required time (0·5—8·0 hours), and then poured on ice (400 g.). The next day, when the decomposition of the acetic anhydride was complete, the product was made alkaline with sodium carbonate and extracted with ether (cf. previous paper). The ether, acetonitrile (if any), and much of the benzene were removed by distillation through Dufton columns. If nitromethane had been used as solvent, potassium hydroxide was added before the ether extraction, and the extract was washed with this reagent (N)—a procedure which was shown in control experiments completely to remove the nitromethane without perceptibly hydrolysing *o*- or *p*-chloro- or -bromo-nitrobenzene. The mixture of products, consisting now of nitrobenzene and halogenobenzene together with small quantities of benzene and halogenonitrobenzenes, was made up to 10 c.c. with absolute methyl alcohol, and measured portions of this solution were taken for the estimations of total nitroxyl and of labile halogen.

*Results.*—The results for chlorobenzene are in Table I(*a*). The conditions of the several groups of experiments are indicated in the side-headings and in col. 2. The quantities of the materials used are at the head of the table and in col. 3. The amounts of nitro-products formed are given in cols. 4 and 5, whilst the ratios of these quantities are in col. 6, and the ratios of the specific rates of nitration in cols. 7 and 8, together with the formal probable errors in the mean values. The nitric acid used in all these experiments was Kahlbaum's, not redistilled. Previous experiments on bromobenzene had shown that the removal of nitrous acid by distillation does not affect the ratio of the rates of nitration [cf. Table I(*b*)].

The results for bromobenzene are given in Table I(*b*). The nitric acid was freshly vacuum-distilled with sulphuric acid before use in Expts. 1—8 and 21—22, but it appears from a comparison of these two groups of experiments with Nos. 8—12 and Nos. 18—20 and 23 respectively that the removal of nitrous acid in this manner makes no marked difference to the relative rates of nitrations.

TABLE I.

*Competitive Nitration of* (a) *Chlorobenzene or* (b) *Bromobenzene and Benzene by Means of Acetyl Nitrate in Solvents.*

Initial Materials: Benzene, 0·0500 g.-mol. Chlorobenzene or bromobenzene, 0·0500 g.-mol. Nitric acid, 0·0375 g.-mol. Acetic anhydride, 0·0375 g.-mol. (initially mixed with the nitric acid). "Solvent" = acetic anhydride additional to the above, or acetonitrile, or nitromethane (quantities tabulated).

| Expt. No. | Time (hrs.). | Solvent (g.-mol.). | Products (g.-mol.). PhNO₂. | Products (g.-mol.). $C_6H_4X{\cdot}NO_2$. | *R*. | $\frac{k_{PhX}}{k_{PhH}}$. | Mean. |
|---|---|---|---|---|---|---|---|
| | | | | (*a*) *Chlorobenzene.* | | | |
| Solvent: Acetic anhydride. Temp.: 0°. | | | | | | | |
| 53 | 1·0 | 0·275 | 0·02270 | 0·000765 | 0·0337 | 0·0255 | 0·0273 ± 0·0006 |
| 54 | ,, | ,, | 0·01942 | 0·000720 | 0·0370 | 0·0294 | |
| 55 | ,, | 0·0207 | 0·02309 | 0·000860 | 0·0372 | 0·0279 | |
| 56 | ,, | ,, | 0·02113 | 0·000718 | 0·0340 | 0·0264 | |
| Solvent: Acetic anhydride. Temp.: 25°. | | | | | | | |
| 57 | 2·0 | 0·275 | 0·01185 | 0·000454 | 0·0384 | 0·0338 | 0·0353 ± 0·0007 |
| 58 | 1·0 | ,, | 0·01763 | 0·000830 | 0·0471 | 0·0384 | |
| 59 | ,, | ,, | 0·01733 | 0·000732 | 0·0423 | 0·0346 | |
| 60 | ,, | ,, | 0·02338 | 0·001066 | 0·0456 | 0·0343 | |
| Solvent: Acetic anhydride. Temp.: 35°. | | | | | | | |
| 61 | 1·0 | 0·275 | 0·01747 | 0·000826 | 0·0474 | 0·0387 | 0·0399 ± 0·0008 |
| 62 | ,, | ,, | 0·01411 | 0·000678 | 0·0480 | 0·0411 | |
| Solvent: Acetonitrile. Temp.: 0°. | | | | | | | |
| 63 | 1·0 | 0·500 | 0·01545 | 0·000475 | 0·0307 | 0·0258 | 0·0257 ± 0·0001 |
| 64 | ,, | ,, | 0·01618 | 0·000498 | 0·0308 | 0·0257 | |
| 65 | ,, | ,, | 0·01603 | 0·000490 | 0·0306 | 0·0255 | |
| Solvent: Acetonitrile. Temp.: 25°. | | | | | | | |
| 66 | 1·0 | 0·500 | 0·02198 | 0·000876 | 0·0398 | 0·0306 | 0·0300 ± 0·0003 |
| 67 | ,, | ,, | 0·02262 | 0·000904 | 0·0399 | 0·0302 | |
| 68 | ,, | ,, | 0·02827 | 0·001210 | 0·0426 | 0·0293 | |
| Solvent: Acetonitrile. Temp.: 35°. | | | | | | | |
| 69 | 1·0 | 0·500 | 0·02523 | 0·01030 | 0·0408 | 0·0328 | 0·0328 |
| Solvent: Nitromethane. Temp.: 0°. | | | | | | | |
| 70 | 0·5 | 0·488 | 0·02166 | 0·000784 | 0·0362 | 0·0278 | 0·0277 ± 0·0005 |
| 71 | 0·8 | ,, | 0·02692 | 0·000998 | 0·0370 | 0·0262 | |
| 72 | 1·0 | ,, | 0·02247 | 0·000862 | 0·0383 | 0·0290 | |
| Solvent: Nitromethane. Temp.: 25°. | | | | | | | |
| 73 | 0·5 | 0·488 | 0·02872 | 0·001380 | 0·0480 | 0·0326 | 0·0312 ± 0·0006 |
| 74 | 1·0 | ,, | 0·02976 | 0·001400 | 0·0472 | 0·0314 | |
| 75 | 1·5 | ,, | 0·03077 | 0·001390 | 0·0453 | 0·0297 | |

| Expt. No. | Time (hrs.). | Solvent (g.-mol.). | Products (g.-mol.). PhNO₂. | $C_6H_4X{\cdot}NO_2$. | R. | $k_{PhX}/k_{PhH}$ | Mean. |
|---|---|---|---|---|---|---|---|
| | | | *(b) Bromobenzene.* | | | | |
| Solvent: Acetic anhydride. Temp.: 0°. | | | | | | | |
| 1 * | 12·0 | 0·275 | 0·00612 | 0·000172 | 0·0281 | 0·0264 | |
| 2 * | 5·5 | ,, | 0·00480 | 0·000126 | 0·0262 | 0·0250 | |
| 3 * | 5·5 | ,, | 0·00427 | 0·000103 | 0·0242 | 0·0258 | |
| 4 * | 8·0 | ,, | 0·00497 | 0·000149 | 0·0300 | 0·0285 | |
| 6 * | 5·0 | 0·207 | 0·00381 | 0·000115 | 0·0303 | 0·0292 | |
| 7 * | 5·5 | ,, | 0·00420 | 0·000127 | 0·0303 | 0·0280 | 0·0261 ± 0·0013 |
| 8 * | 8·5 | ,, | 0·00498 | 0·000127 | 0·0255 | 0·0242 | |
| 9 | 1·0 | 0·275 | 0·0207 | 0·000659 | 0·0318 | 0·0248 | |
| 10 | ,, | ,, | 0·0207 | 0·000667 | 0·0322 | 0·0250 | |
| 11 | ,, | ,, | 0·0157 | 0·000479 | 0·0304 | 0·0255 | |
| 12 | ,, | ,, | 0·0234 | 0·000722 | 0·0309 | 0·0234 | |
| Solvent: Acetic anhydride. Temp.: 25°. | | | | | | | |
| 13 | 1·0 | 0·275 | 0·01745 | 0·000673 | 0·0386 | 0·0317 | |
| 14 | ,, | ,, | 0·01755 | 0·000700 | 0·0399 | 0·0326 | 0·0320 ± 0·0003 |
| 15 | ,, | ,, | 0·0176 | 0·000687 | 0·0391 | 0·0318 | |
| 16 | ,, | ,, | 0·0155 | 0·000588 | 0·0380 | 0·0318 | |
| Solvent: Acetic anhydride. Temp.: 35°. | | | | | | | |
| 18 | 1·0 | 0·275 | 0·0115 | 0·000441 | 0·0387 | 0·0340 | |
| 19 | ,, | ,, | 0·00621 | 0·000220 | 0·0354 | 0·0334 | |
| 20 | ,, | ,, | 0·0129 | 0·000503 | 0·0391 | 0·0340 | 0·0339 ± 0·0002 |
| 21 * | ,, | ,, | 0·00868 | 0·000316 | 0·0365 | 0·0333 | |
| 22 * | ,, | ,, | 0·0108 | 0·000412 | 0·0383 | 0·0341 | |
| 23 | ,, | ,, | 0·0163 | 0·000676 | 0·0413 | 0·0343 | |
| Solvent: Acetonitrile. Temp.: 0°. | | | | | | | |
| 24 | 0·5 | 0·500 | 0·00523 | 0·000141 | 0·0270 | 0·0255 | |
| 25 | 1·0 | ,, | 0·01355 | 0·000394 | 0·0290 | 0·0255 | |
| 26 | 2·0 | ,, | 0·0131 | 0·000385 | 0·0294 | 0·0254 | |
| 27 | ,, | ,, | 0·0157 | 0·000462 | 0·0293 | 0·0245 | 0·0247 ± 0·0003 |
| 28 | 4·0 | ,, | 0·0147 | 0·000386 | 0·0262 | 0·0223 | |
| 29 | ,, | ,, | 0·0163 | 0·000485 | 0·0296 | 0·0247 | |
| 30 | 5·0 | ,, | 0·01815 | 0·000555 | 0·0305 | 0·0247 | |
| Solvent: Acetonitrile. Temp.: 25°. | | | | | | | |
| 31 | 1·0 | 0·500 | 0·01935 | 0·000671 | 0·0347 | 0·0276 | |
| 32 | ,, | ,, | 0·01955 | 0·000685 | 0·0351 | 0·0278 | |
| 33 | ,, | ,, | 0·0192 | 0·000704 | 0·0366 | 0·0293 | 0·0291 ± 0·0005 |
| 34 | 2·0 | ,, | 0·02165 | 0·000882 | 0·0407 | 0·0313 | |
| 35 | ,, | ,, | 0·0217 | 0·000835 | 0·0385 | 0·0296 | |
| Solvent: Acetonitrile. Temperature: 35°. | | | | | | | |
| 36 | 0·5 | 0·500 | 0·0210 | 0·000852 | 0·0406 | 0·0316 | |
| 37 | ,, | ,, | 0·02045 | 0·000824 | 0·0401 | 0·0316 | 0·0322 ± 0·0004 |
| 38 | 1·0 | ,, | 0·0250 | 0·00114 | 0·0457 | 0·0333 | |
| Solvent: Nitromethane. Temp.: 0°. | | | | | | | |
| 39 | 0·5 | 0·488 | 0·0255 | 0·000811 | 0·0318 | 0·0229 | 0·0230 ± 0·0001 |
| 40 | 1·5 | ,, | 0·0274 | 0·000915 | 0·0334 | 0·0232 | |
| Solvent: Nitromethane. Temp.: 35°. | | | | | | | |
| 41 | 0·5 | 0·488 | 0·0293 | 0·00129 | 0·0440 | 0·0297 | 0·0295 ± 0·0001 |
| 42 | 1·0 | ,, | 0·0304 | 0·00135 | 0·0444 | 0·0294 | |

* Freshly distilled nitric acid of very low nitrous acid content employed.

The formal probable errors in the means of the rate ratios obtained in the different sets of experiments are only a few units %, and it therefore appears that the results are accurate enough for the study of effects due to conditions, since these effects are usually a good deal greater. We collect the mean ratios into the synoptic Table II. It will be seen that chlorobenzene is nitrated 25—39 times, and bromobenzene 29—43 times, more slowly than benzene; so that under corresponding conditions bromobenzene is nitrated a little more slowly than chlorobenzene, the mean difference being about 10%. The effect of solvents on the rate ratios is small and not very regular: the three solvents investigated do not stand in the

same order for chloro- and bromo-benzene. The effect of temperature on the ratios, however, is well marked: the ratios always rise (approach unity) when the temperature is raised, and the ratio in which they change is more than proportional to the increase in the absolute temperature.

TABLE II.

*Synopsis of the Ratios for Chloro- and Bromo-benzene.*

| | $k_{PhCl}/k_{PhH}$. | | | $k_{PhBr}/k_{PhH}$. | | |
|---|---|---|---|---|---|---|
| Temp. | $Ac_2O$. | $CH_3$·CN. | $CH_3$·$NO_2$. | $Ac_2O$. | $CH_3$·CN. | $CH_3$·$NO_2$. |
| 0° | 0·0273 | 0·0257 | 0·0277 | 0·0261 | 0·0247 | 0·0230 |
| 25 | 0·0353 | 0·0300 | 0·0312 | 0·0320 | 0·0291 | — |
| 35 | 0·0399 | 0·0328 | — | 0·0339 | 0·0322 | 0·0295 |

(2) *Orientation in the Nitration of Chorobenzene and Bromobenzene by Acetyl Nitrate in Various Solvents.*

We have not carried out a very full investigation of orientation in the nitration of chloro- and bromo-benzene under the conditions used in the competitive nitrations for the following reasons. A detailed investigation of orientation in the nitration of toluene and of ethyl benzoate in homogeneous media was recorded in Parts II and III. The results may be compared with those obtained by Holleman for nitration by means of nitric acid without a solvent. The comparison shows that the orientation percentages are only slightly sensitive to changes in the nitrating agent and the medium; so it would have made no significant difference if we had calculated the factors expressing the effect of the original substituents on the probability of substitution in the several nuclear positions by means of our rate ratios and Holleman's orientational data interpolated to the proper temperatures, instead of specially determining the orientational proportions under conditions strictly corresponding to those of the rate experiments. Furthermore Holleman's results show, and ours for toluene as far as they go confirm, that when the temperature is changed the proportions of isomerides exhibit a shift which is in the direction, and of about the magnitude, of the shift calculated by the theory of Scheffer (*Proc. K. Akad. Wetensch. Amsterdam*, 1913, **15**, 118; cf. Bradfield and Jones, J., 1928, 1006, 3073); so that, for the purpose of reducing orientational data to the correct temperature for combination with the rate ratios we might without any real loss of accuracy have used the theory, thus avoiding numerous experiments.

We felt that it was not entirely safe to assume that these possible simplifications, which are easy to see in retrospect, can be applied in new examples, and we have therefore carried out a skeleton study of orientation in the homogeneous nitration of chloro- and bromobenzene. This work makes it quite clear that, in these cases also, the effects arising from a change in the nitrating medium are small, and those due to changes of temperature can be predicted sufficiently accurately from either Scheffer's theory or Holleman's results.

*Analysis.*—Thermal analysis was adopted, clearing points rather than freezing points being employed, however, as is now usual for binary mixtures. Artificial mixtures of *o*- and *p*-chloronitrobenzene and of *o*- and *p*-bromonitrobenzene containing no other compound could be analysed with an accuracy of 0·2%.

The separation of mixtures of *o*- and *p*-chloro- or -bromo-nitrobenzene from accompanying halogeno- and 2 : 4-dinitrohalogeno-benzene was effected by distillation under reduced pressure, controlled, on the one hand, by estimations of nitroxyl with the aid of titanous chloride, and on the other, by m. p.'s. Analysis following such a separation involved errors up to 1%.

*Nitration.*—A mixture of nitric acid (0·3 g.-mol.) and acetic anhydride (0·3 g.-mol.), prepared at 0°, was added with stirring to a solution of the halogenobenzene (0·2 g.-mol.) in the solvent (90 c.c.) at the necessary temperature. The "solvent" was either more acetic anhydride, or acetonitrile or nitromethane, and the temperature was 0° or 25°. The product was worked up, as for the competitive nitrations (except that here no benzene had to be removed), and the mononitro-compounds were isolated and analysed as described above.

*Results.*—These are given in the last two sections of Table III under the side-heading "This paper." Each recorded figure is the mean of duplicate experiments, which were concordant to within (usually well within) 1%. The observations on chlorobenzene were

made by Dr. W. M. Morgans, to whom we are indebted for his collaboration. The remainder of the table is occupied by Holleman's results and those of this series for toluene and ethyl benzoate, and Holleman's values for chloro- and bromo-benzene, in illustration of the foregoing remarks on the influence of changes of the nitrating medium on the orientation of the reaction.

TABLE III.

*Effect of Changes of Nitration Medium and Temperatures on the Orientation of Substitution, and New Results for Orientation in the Homogeneous Nitration of Chlorobenzene and Bromobenzene.*

| Ref. | Nitration medium. | Temp. | Proportions of isomerides (%). | | |
|---|---|---|---|---|---|
| | | | *o*-. | *m*-. | *p*-. |
| *Toluene.* | | | | | |
| Holleman | $HNO_3$ (heterogeneous) | − 30° | 55·6 | 2·7 | 41·7 |
| ,, | ,, ,, | 0 | 56·0 | 3·1 | 40·9 |
| ,, | ,, ,, | + 60 | 57·5 | 4·0 | 38·5 |
| Part II | $AcNO_3$ in $Ac_2O$ | 0 | 58·1 | 3·7 | 38·2 |
| ,, | ,, ,, | + 30 | 58·4 | 4·4 | 37·2 |
| ,, | $HNO_3$ in $MeNO_2$ | + 30 | 58·5 | 4·4 | 37·1 |
| *Ethyl benzoate.* | | | | | |
| Holleman | $HNO_3$ (heterogeneous) | − 40 | 25·5 | 73·2 | 1·3 |
| ,, | ,, ,, | 0 | 28·3 | 68·4 | 3·3 |
| ,, | ,, ,, | + 30 | 27·7 | 66·4 | 5·9 |
| Part III | $AcNO_3$ in $Ac_2O$ | + 18 | 24·1 | 72·0 | 4·0 |
| *Chlorobenzene.* | | | | | |
| Holleman | $HNO_3$ (heterogeneous) | − 30 | 26·9 | 0·0 | 73·1 |
| ,, | ,, ,, | 0 | 30·1 | 0·0 | 69·9 |
| This paper | $AcNO_3$ in MeCN | 0 | 28·8 | 0·0 | 71·2 |
| ,, | ,, ,, ,, | + 25 | 30·2 | 0·0 | 69·8 |
| ,, | ,, ,, $MeNO_2$ | 0 | 29·0 | 0·0 | 71·0 |
| ,, | ,, ,, ,, | + 25 | 30·2 | 0·0 | 69·8 |
| *Bromobenzene.* | | | | | |
| Holleman | $HNO_3$ (heterogeneous) | − 30 | 34·4 | 0·0 | 65·6 |
| ,, | ,, ,, | 0 | 37·6 | 0·3 | 62·1 |
| This paper | $AcNO_3$ in $Ac_2O$ | 0 | 38·5 | 0·0 | 61·5 |
| ,, | ,, ,, ,, | + 25 | 42·0 | 0·0 | 58·0 |

For the purpose of calculating the factors by which the chlorine and bromine atoms in chloro- and bromo-benzene change the rate of nitration in the different nuclear positions of these molecules, we shall, in view of the above discussion and the data in Table III, adopt certain values for the orientation proportions obtaining in homogeneous nitration. These adopted values are in Table IV. They are obtained from the new observations recorded in Table III by, first, disregarding the small and uncertain effects of changes of solvent, and secondly, smoothing the temperature effect, partly with the aid of Holleman's more numerous data for the temperature dependence of orientation, and partly by means of Scheffer's relation.

TABLE IV.

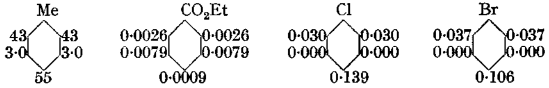
*Percentages of Isomerides formed in the Nitration of Chloro- and Bromo-benzene by Acetyl Nitrate.*

| Temp. | Chlorobenzene. | | Bromobenzene. | |
|---|---|---|---|---|
| | *o*-. | *p*-. | *o*-. | *p*-. |
| 0° | 28·2 | 71·8 | 39·0 | 61·0 |
| 25 | 31·0 | 69·0 | 41·4 | 58·6 |
| 35 | 32·1 | 67·9 | 42·4 | 57·6 |

### (3) *Partial Rate Factors for the Nitration of Chlorobenzene and Bromobenzene by Acetyl Nitrate.*

A partial rate factor is the factor by which the orienting substituent changes the specific rate of substitution in an individual nuclear position. The partial rate factors for the

nitration of chloro- and bromo-benzene can be calculated from the velocity and orientational data of Sections 1 and 2. The rate ratios have simply to be multiplied by orientational fractions (percentages divided by 100) and certain statistical factors, *viz.*, 3 for ortho- and 6 for para-positions. The factors thus calculated for the ortho- and para-nitration of chloro- and bromo-benzene in the three solvents and at the three temperatures used are given in Table V. For comparison with former results we can interpolate the data for acetic anhydride as solvent to 18°, the temperature at which the nitration of ethyl benzoate was examined in this solvent. We thus obtain the comparisons shown in the following formulæ :




The figures illnstrate what is already known qualitatively (Part I, *loc. cit.*), *viz.*, that, although substituents of class 3 are *op*-orienting like those of class 1, yet the former work by differential deactivation and not as in class 1 by differential activation ; the opposite kind of differential deactivation leads to the *m*-orientation of class 2.

TABLE V.

*Partial Rate Factors for the Nitration of Chloro- and Bromo-benzene by Acetyl Nitrate.*

| | Chlorobenzene. | | | Bromobenzene. | | |
|---|---|---|---|---|---|---|
| Temp. | $Ac_2O$. | $CH_3$·CN. | $CH_3$·$NO_2$. | $Ac_2O$. | $CH_3$·CN. | $CH_3$·$NO_2$. |
| *Ortho-position.* | | | | | | |
| 0° | 0·0231 | 0·0217 | 0·0235 | 0·0305 | 0·0289 | 0·0269 |
| 25 | 0·0329 | 0·0280 | 0·0291 | 0·0397 | 0·0361 | — |
| 35 | 0·0385 | 0·0317 | — | 0·0431 | 0·0409 | 0·0375 |
| *Para-position.* | | | | | | |
| 0 | 0·118 | 0·110 | 0·120 | 0·0955 | 0·0904 | 0·0842 |
| 25 | 0·146 | 0·124 | 0·129 | 0·112 | 0·102 | — |
| 35 | 0·162 | 0·135 | — | 0·117 | 0·111 | 0·102 |

*The Temperature Effect.*—Concerning the effects of conditions, the partial rate factors are seen to vary with the solvent, though neither largely nor very regularly. They vary both largely and regularly with the temperature, however, increasing as the temperature is raised. The change between 0° and 35° is in a number of cases of the order of 50%, and it is generally greater for the smaller partial rate factors than for the larger ones. Qualitatively, this is the type of variation which would be obtained if the orienting substituent affected the rates of reaction at the several nuclear positions by changing the energies, rather than the entropies, of activation. We can form an estimate of the extent to which this happens, because, if *only* the energy were changed, then, $F$ being a partial rate factor, $-T \log F$ should be independent of temperature. Corresponding to the values of $F$ in Table V, values of $-T \log F$ are set out in Table VI. They are constant enough to enable us to

TABLE VI.

*Values of* $-$T *log* F *for the Nitration of Chloro- and Bromo-benzene by Acetyl Nitrate.*

| | Chlorobenzene. | | | Bromobenzene. | | |
|---|---|---|---|---|---|---|
| Temp. | $Ac_2O$. | $CH_3$·CN. | $CH_3$·$NO_2$. | $Ac_2O$. | $CH_3$·CN. | $CH_3$·$NO_2$. |
| *Ortho-position.* | | | | | | |
| 0° | 447 | 454 | 445 | 414 | 421 | 430 |
| 25 | 443 | 462 | 456 | 418 | 430 | — |
| 35 | 436 | 462 | — | 421 | 428 | 439 |
| *Para-position.* | | | | | | |
| 0 | 254 | 261 | 252 | 279 | 286 | 294 |
| 25 | 250 | 270 | 265 | 282 | 295 | — |
| 35 | 244 | 269 | — | 287 | 295 | 305 |

conclude that at least the main effect of the original substituent is on the energy of activation. For instance, between 0° and 35° the absolute temperature is varied over a range of 13%; but the average variation of $-T \log F$ between the same two temperatures is only 2·5%. This latter variation exceeds the experimental error in the determination of $F$, but there can be no doubt that $F$ varies with $T$ in such a way that most of the change in $T$ is compensated by an opposite change in $-\log F$; the fact that this compensation is nearly complete means that nearly the whole effect of the substituent is concerned with the energy of activation of substitution in the several nuclear positions.

(4) *Relative Rates of Nitration of Fluorobenzene and Benzene by Means of Acetyl Nitrate in Acetic Anhydride and Acetonitrile at 0°, 25°, and 35°.*

Our work on fluoro- and iodo-benzene is less accurate than the foregoing; indeed, that on iodobenzene is hardly more than qualitative. It should be emphasised that for neither of these two halides do we claim to establish standard values with regard to their rates of nitration, and our only reason for including reports of the experiments is that they appear to establish a remarkable relationship between the rates of reaction of the four phenyl halides.

In the case of fluorobenzene our method (for purely practical reasons) was to carry out competitive nitrations of fluorobenzene and bromobenzene. Having thus determined the ratio of the rates of nitration of these substances, we could relate the rate of nitration of fluorobenzene to that of benzene with the aid of the known relation between the rates of nitration of bromobenzene and benzene.

*Analysis.*—In these competitive nitrations the analytical method was in principle known, since the fluorobenzene simply took the place of the benzene in the previously studied competitive nitrations of bromobenzene and benzene. Total nitroxyl was determined by reduction with titanous chloride. Bromonitrobenzenes were determined by alcoholysis of the total halogenonitrobenzenes, and subsequent estimation of the bromide ion. The difference of the two values represents the fluoronitrobenzenes. These processes were checked with satisfactory results by using artificial mixtures.

*Nitrations.*—Fluorobenzene was prepared by Balz and Schiemann's method (*Ber.*, 1927, **60**, 1186) as modified by Le Fèvre and Turner (J., 1930, 1160), and was carefully fractionated.

"Dummy" nitrations, carried out to test the effect of solvent nitration on the estimated proportion of fluoronitrobenzene, showed that this error, although much larger than for the competitions between benzene and bromobenzene, did not amount to more than a few units %.

The general method of nitration was as follows. A mixture of nitric acid (0·0187 g.-mol.) and acetic anhydride (0·0187 g.-mol.) was made at 0° and diluted with the solvent (excess of acetic anhydride or acetonitrile, usually 3 c.c.). This was added with mechanical stirring to a solution of fluorobenzene (0·025 g.-mol.) and bromobenzene (0·025 g.-mol.) in the same solvent (usually 10 c.c.) at the required temperature (0°, 25°, or 35°), and the mixture was kept at this temperature for the necessary time (0·5—1·0 hour), and then poured on ice. After the hydrolysis of the acetic anhydride, the aromatic products were extracted with ether and the extract was well washed with water, urea solution, water, nitron acetate solution, and water successively. This procedure was adopted, instead of extraction from an alkaline solution, because the fluoronitrobenzenes are rather easily hydrolysed.

The urea and nitron washings were tested for nitroxyl by means of titanous chloride: the amount found was usually less than 1% of the aromatically bound nitroxyl. In some experiments the ethereal extract was also washed with sodium hydrogen carbonate solution, which was subsequently found to contain very little nitroxyl. By working through all these processes with solutions of *o*- and *p*-fluoronitrobenzenes in nitric-acetic anhydride, it was ascertained that not more than 2% of the fluoronitro-compounds is lost by hydrolysis. The extract was finally dried and distilled through Dufton columns, in order to remove ether and some of the fluorobenzene, and the residue was analysed for nitroxyl and alcoholysable bromine as described. In one experiment the bromobenzene was replaced by chlorobenzene.

*Results.*—These are in Table VII, the arrangement of which corresponds to that of Table I, except that the figures in the last column are calculated from those in the column before

with the aid of the ratios of Table II. In all experiments the nitric acid used was Kahlbaum's, and it was not redistilled.

TABLE VII.

*Competitive Nitration of Fluorobenzene and Bromobenzene (or Chlorobenzene) by Means of Acetyl Nitrate in Solvents.*

Initial Materials: Fluorobenzene, 0·0250 g.-mol. Bromobenzene (or chlorobenzene), 0·0250 g.-mol. Nitric acid, 0·0187 g.-mol. Acetic anhydride, 0·0187 g.-mol. (initially mixed with the nitric acid). "Solvent" = acetic anhydride additional to the above, or acetonitrile (quantities tabulated).

| Expt. No. | Time (hrs.). | Solvent (g.-mol.). | Products (g.-mols.). $C_6H_4Br{\cdot}NO_2$. | $C_6H_4F{\cdot}NO_2$. | $R$. | $\frac{k_{PhF}}{k_{PhBr}}$. | $\frac{k_{PhF}}{k_{PhH}}$. |
|---|---|---|---|---|---|---|---|
| Solvent: Acetic anhydride. Temp.: 0°. | | | | | | | |
| 85 | 1·0 | 0·139 | 0·000692 | 0·00362 | 5·23 | 5·57 | 0·145 |
| 86 | ,, | ,, | 0·000540 | 0·00292 | 5·39 | 5·68 | 0·148 |
| 87 | 0·5 | ,, | 0·000391 | 0·00221 | 5·65 | 5·87 | 0·153 |
| 88* | 1·0 | ,, | 0·000968† | 0·00503 | 5·20 | 5·69 | 0·155 |
| Solvent: Acetic anhydride. Temp.: 25°. | | | | | | | |
| 90 | 1·0 | 0·139 | 0·000625 | 0·00310 | 4·96 | 5·23 | 0·167 |
| 91 | ,, | ,, | 0·000974 | 0·00459 | 4·71 | 5·10 | 0·163 |
| Solvent: Acetic anhydride. Temp.: 35°. | | | | | | | |
| 92 | 1·0 | 0·139 | 0·000652 | 0·00276 | 4·23 | 4·43 | 0·150 |
| 93 | ,, | ,, | 0·000931 | 0·00393 | 4·22 | 4·51 | 0·153 |
| 94 | 0·5 | ,, | 0·000361 | 0·00154 | 4·26 | 4·37 | 0·148 |
| 95 | 1·0 | ,, | 0·000636 | 0·00300 | 4·72 | 5·15 | 0·174 |
| 96 | ,, | ,, | 0·000208 | 0·00101 | 4·85 | 4·93 | 0·167 |
| Solvent: Acetonitrile. Temp.: 0°. | | | | | | | |
| 99 | 1·0 | 0·250 | 0·000735 | 0·00377 | 5·13 | 5·48 | 0·135 |
| 100 | ,, | ,, | 0·000745 | 0·00379 | 5·09 | 5·44 | 0·134 |
| Solvent: Acetonitrile. Temp.: 25°. | | | | | | | |
| 101 | 1·0 | 0·250 | 0·001497 | 0·00650 | 4·34 | 4·88 | 0·142 |
| 102 | ,, | ,, | 0·001710 | 0·00661 | 3·87 | 4·32 | 0·126 |
| Solvent: Acetonitrile. Temp.: 35°. | | | | | | | |
| 103 | 1·0 | 0·250 | 0·001919 | 0·00838 | 4·36 | 5·11 | 0·164 |
| 104 | ,, | ,, | 0·002040 | 0·00859 | 4·21 | 4·94 | 0·158 |

* Chlorobenzene used in place of bromobenzene. † $C_6H_4Cl{\cdot}NO_2$.

A synopsis of the mean ratios, $k_{PhF}/k_{PhH}$, is given in Table VIII. It will be observed that the variation with temperature is not regular. In view of the regularity of the temperature effect in the more accurately investigated rate-ratios for chloro- and bromobenzene, we take this to mean that the results for fluorobenzene are only semi-quantitative, any of the values recorded being subject to a possible error of the order of 10%.

TABLE VIII.

*Synopsis of the Rate Ratios for Fluorobenzene.*

| Solvent. | $k_{PhF}/k_{PhH}$. 0°. | 25°. | 35°. |
|---|---|---|---|
| Acetic anhydride | 0·149 | 0·165 | 0·158 |
| Acetonitrile | 0·134 | 0·134 | 0·161 |

(5) *Relative Rates of Nitration of Iodobenzene and Benzene by Means of Acetyl Nitrate.*

Our few experiments on the competitive nitration of iodobenzene and benzene were carried out by the methods described in Section 1, but, as the analytical method, which worked so satisfactorily in those experiments, gave very poor results in the present example, our data have little quantitative value. Nevertheless, they seem to establish the qualitative relations referred to in Section 6.

*Analysis.*—No difficulty was experienced in the estimation by the use of titanous chloride of nitroxyl in mixtures of *o*- and *p*-iodonitrobenzenes, alone or mixed with benzene, nitrobenzene,

and iodobenzene. The estimation of iodonitrobenzenes by methyl-alcoholysis was, however, unsatisfactory : it tended to give slightly low results with the iodonitrobenzenes themselves, and very high results (up to 15% high) when these substances were treated in admixture with excess of iodobenzene and nitrobenzene, notwithstanding that iodobenzene did not appear to be more than slightly alcoholysed when treated alone with the same reagent. In spite of this we used the method, as there was no intention at the time of seeking more than the order of magnitude of the rate ratio.

*Nitration.*—Nitrations were carried out, and the products worked up, just as for the competitive nitrations of chlorobenzene and benzene (Section 1).

*Results.*—These are in Table IX. The values of $k_{PhI}/k_{PhH}$ are within the range 0·1—0·3, and in spite of the generally poor consistency, may be taken to indicate an order of magnitude of 0·2, no distinctions being possible with respect to temperature and solvent.

TABLE IX.

*Competitive Nitration of Iodobenzene and Benzene by Means of Acetyl Nitrate in Solvents.*

Initial Materials: Benzene, 0·0500 g.-mol. Iodobenzene, 0·0500 g.-mol. Nitric acid, 0·0375 g.-mol. Acetic anhydride, 0·0375 g.-mol. (initially mixed with the nitric acid). "Solvent" = acetic anhydride additional to the above, or acetonitrile (quantities tabulated).

| Expt. No. | Time (hrs.). | Solvent (g.-mol.). | Products (g.-mols.). $PhNO_2$. | $C_6H_4I{\cdot}NO_2$. | *R*. | $k_{PhI}/k_{PhH}$. |
|---|---|---|---|---|---|---|
| *Solvent : Acetic anhydride. Temp. : 0°.* | | | | | | |
| 76* | 1·0 | 0·275 | 0·00089 | 0·000154 | 0·173 | 0·172 |
| 77* | 8·0 | ,, | 0·00177 | 0·000248 | 0·140 | 0·138 |
| 78 | 1·0 | ,, | 0·00532 | 0·000620 | 0·116 | 0·111 |
| 79 | ,, | ,, | 0·00110 | 0·000302 | 0·273 | 0·271 |
| Solvent : Acetic anhydride. Temp. : 25°. | | | | | | |
| 80 | 1·0 | 0·275 | 0·00644 | 0·000120 | 0·187 | 0·177 |
| *Solvent : Acetic anhydride. Temp. : 35°.* | | | | | | |
| 82 | 1·0 | 0·275 | 0·00309 | 0·000708 | 0·229 | 0·223 |
| Solvent : Acetonitrile. Temp. : 25°. | | | | | | |
| 83 | 1·0 | 0·500 | 0·0121 | 0·00346 | 0·284 | 0·258 |

* Freshly distilled nitric acid of low nitrous acid content used.

### (6) *Relative Rates of Nitration of the Four Halogenobenzenes.*

From the results of Sections (1), (4), and (5), we can compare the rates of nitration of the halogenobenzenes under constant conditions, *e.g.*, for nitration by means of acetyl nitrate in acetic anhydride as solvent at 18° :

| | PhF. | PhCl. | PhBr. | PhI. |
|---|---|---|---|---|
| Nitration rate (PhH = 1) ..................... | 0·15 | 0·033 | 0·030 | ~0·18 |

The rate passes through a minimum, and although both the extremes of the series need further investigation, it seems unlikely that future experiments will change the qualitative result.* We may therefore consider its significance.

In the theory of organic reactions it is recognised that in the most general case a group can exert four distinct polar effects; these comprise two polarisations, termed (1) the inductive, and (2) the mesomeric, effect, and two polarisabilities, *viz.*, (3) the inductomeric, and (4) the electromeric, effect. The two polarisabilities (3) and (4) may be disregarded in considerations of chemical equilibria, which depend only on unenergised ground states. Effects (2) and (4), which depend on conjugation, can be excluded unless the appropriate unsaturation is present.

The order of the halogens with respect to these polar effects has already been con-

* The qualitative relations, PhH ≫ PhF ~ PhI ≫ PhCl > PhBr, are confirmed in the next paper, which describes an investigation by a different method.

siderably discussed, and much that was obscure has been cleared up by the work of Bennett and of Branch particularly. As the rather voluminous literature of the subject can easily be traced through the more recent papers by these authors (since 1933), we do not here review it, but merely summarise the accepted conclusions. These are as follows. (1) From the influence on chemical equilibria of halogens in saturated aliphatic combination, it follows that the inductive effect of halogens is electron-attracting ($-I$), as it should be theoretically, and is in the order F > Cl > Br > I. (2) From the influence on chemical equilibria of *op*-halogens in direct combination with the benzene ring, it follows that the mesomeric effect of halogens is electron-repelling ($+M$), as it must be theoretically, and is in the order F > Cl > Br > I. (3) The last-named group of equilibria show that the *differential* mesomeric effect amongst the halogens so far outweighs the differential inductive effect that processes which require an increased electron-density at the reaction site are suppressed least by fluorine and most by iodine, an inversion of the relationship which would obtain if the differential inductive effect controlled the order. These three conclusions account for the whole of the observations of the effects of halogens on equilibria.

The interpretation of the influence of halogens on reaction velocity is complicated by the additional presence of polarisability effects. The data hitherto considered in this connexion relate practically exclusively to the influence of halogens directly bound to the benzene ring on reactions in an aromatic side chain. For such examples we must expect both polarisabilities, the inductomeric and the electromeric effects, to contribute to the observed result. Actually, the observed result is remarkably uniform: as before, reactions which require electrons to be supplied are suppressed, least by fluorine and most by iodine; and correspondingly, those that want electrons withdrawn are assisted, least by fluorine and most by iodine. It follows that, whatever the polarisability effects may be doing quantitatively in these examples, they are not qualitatively upsetting the relationships which would in their absence have been established by the polarisations. It will be suggested below that this is because the polarisability effects are too weak.

Our experiments bring data of another type into the field under review: they relate to the effect of aromatically bound halogens on a *nuclear* reaction—one which strongly demands electrons. Here we find the old uniformity upset: the sequence determined by a dominating differential mesomeric effect has partly reverted to that which would be produced by the inductive effect if the mesomeric effect disappeared. Now we cannot, of course, suppose that the mesomeric effect does, even partly, disappear: like the inductive effect, it is a permanent property of the molecule. The observed disturbance must therefore be attributed to the incursion of polarisability effects, which, for nuclear substitution, in contrast to side-chain reactions, are strong enough to become qualitatively evident. The observed result would be explained if the extra effect due to the polarisabilities were an electron-release, as theoretically it must be, and were in the order I > Br > Cl > F.

It is not an unexpected conclusion that polarisability effects are more prominent in aromatic nuclear than in side-chain reactions; for in nuclear reactions, the reagent, whose field excites polarisability effects, comes in closer proximity to the influencing group. Furthermore, in ortho- and para-substitution, with which alone we are concerned in the nitration of halogenobenzenes, the reagent attacks positions particularly favourable to the excitation of a strong electromeric effect. Apart from any special cases, the electromeric effect is recognised to be generally prominent in aromatic nuclear substitution, which forms one of the best known illustrations of its distinctive operation. It was, for instance, shown in Part I that the two polar effects whose co-existence is essential in the interpretation of the connexion between orientation and reaction rate are inductive polarisation and electromeric polarisability with their fundamentally distinctive time relations.

Therefore we interpret our results as making it probable that the modification attributed to increased polarisability is due mainly to increased electromeric polarisability; and that the sequence given above for the total polarisability effect is the sequence for the electromeric effect ($+E$): I > Br > Cl > F. Bennett has assumed the opposite sequence on the grounds that the electromeric and mesomeric effects "have a common origin" (J., 1935, 1830), but we cannot see that common origins necessitate common behaviour; for example, mesomeric energy and polarisation have a common origin but are far from parallel in be-

haviour. Nevertheless it must be admitted that the conclusions to which our experiments inevitably lead relate only to the total polarisability effect, and that in specialising these conclusions to the electromeric effect we also are supplementing deduction by personal judgement.

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# 177. *Influence of Directing Groups on Nuclear Reactivity in Oriented Aromatic Substitutions. Part V. A Dilatometric Investigation of the Kinetics of Aromatic Nitration especially in Nitromethane Solution.*

By Gilbert A. Benford and Christopher K. Ingold.

By the use of tapless dilatometers, a general survey has been made of the kinetics of aromatic nitration in various solvents, in which the rates vary over a wide range; and also a detailed study of nitration in nitromethane, a solvent giving intermediate rates. Nitric acid was always employed in large, effectively constant, excess. Benzene and several derivatives were investigated.

The nitration of benzene was a reaction of order zero. It was retarded by nitrous acid according to the law $k_0 = 1/(a + b\sqrt{n})$, where $n$ is the concentration of nitrous acid. The parameters $a$ and $b$ were determined as power functions of the nitric acid concentration, $N$, and exponential functions of the temperature, $\theta$.

The nitrations of toluene and of ethylbenzene were also reactions of order zero, with absolute rates always equal to each other and to the rate of nitration of benzene for the same $n$, $N$, and $\theta$.

For the halogenobenzenes the rates were smaller than for benzene and its homologues in two degrees, a lower degree for fluoro- and iodo-benzene, and a higher degree for chloro- and bromo-benzene (H > F, I > Cl,Br). The effective reaction order was greater than zero in two degrees, with the same distribution of the compounds (0 = H < F, I < Cl,Br). The effective reaction order always increased as the reaction proceeded, approaching, in the cases of chloro- and bromo-benzene very closely approaching, unity *towards the end of a run. The variations of rate with n and N were qualitatively* similar to those observed with benzene.

All these facts can be explained by, and indeed seem to necessitate, the chain-reaction mechanism formulated on p. 954.

It is suggested that the efficiency of nitrating agents $X{\cdot}NO_2$ increases with the electron-affinity of X.

## (Sections 1—4). Methods and Survey of Solvents.

### (1) *Relation of the Present to Previous Work.*

(a) *Objects of the Investigation.*—The present work had two objects The first was to develop a convenient general method for studying the kinetics of the nitration of aromatic substances, the methods hitherto described leaving much to be desired. This problem was solved by the elaboration of a dilatometric method capable of wide application.

The second was to find the kinetic laws governing the nitration of benzene and of some of its simpler derivatives under the same experimental conditions: it is remarkable that the kinetics of the nitration of benzene have never yet been elucidated under any conditions. This aim has been fulfilled to the following extent. The dilatometric method was first employed in a brief survey of nitration in various solvents; nitromethane was then chosen as a solvent suitable for further investigation. For this solvent, the nitration of benzene was studied in detail; the kinetic laws were established, and the mechanism of the reaction was elucidated. It proved to be a chain reaction, and we are able to specify in considerable detail the modes of origin, propagation, and extinction of the chains. The nitration of certain benzene derivatives was then examined; for toluene and ethylbenzene the kinetic

laws were exactly established, just as for benzene, whilst for the four halogenobenzenes they were qualitatively elucidated. The mechanism, which had been established for the nitration of benzene, was shown to be general amongst these derivatives.

Corresponding to these two objects, we give two brief historical sketches, the subjects treated not having previously been summarised in the literature.

(b) *Previous Work on Dilatometry in Reaction Kinetics.*—Dilatometry was first shown to be applicable to the study of reaction kinetics by Knöfler (Diss., Erlangen, 1888). The form of dilatometer used by him, and by the majority of subsequent investigators (Koelichen, *Z. physikal. Chem.*, 1900, **3**, 489; Galeotti, *ibid.*, 1911, **76**, 105; 1912, **89**, 241; Wright, P., 1913, **29**, 280; Aberlof, *J. Amer. Chem. Soc.*, 1926, **48**, 3048; 1927, **49**, 2957; Murphy, *ibid.*, 1931, **53**, 978; Brönsted *et al.*, *ibid.*, 1927, **49**, 2562; 1929, **51**, 431; 1930, **52**, 1394; *Trans. Faraday Soc.*, 1929, **25**, 59; Sreenivasaya and Sastri, *Biochem. J.*, 1929, **23**, 975; Rona and Lemmer, *Biochem. Z.*, 1931, **235**, 214; Hoather and Goodeve, *Trans. Faraday Soc.*, 1934, **30**, 626), consisted essentially of a bulb with a capillary tube at the top, and a tap at the bottom for filling. This tap has been a frequent source of trouble, since its unprotected presence restricts dilatometry to liquids which do not attack or dissolve tap-grease: a minute leak is sufficient to upset the readings. The difficulty is the same if a ground stopper is used in place of the tap (Duane, *Amer. J. Sci.*, 1901, **11**, 349; Palomaa and Salomon, *Ber.*, 1934, **67**, 424), and a rubber stopper (Riiber, *Ber.*, 1922, **55**, 3132) seems hardly a satisfactory substitute. Two methods have been tried for overcoming this difficulty. One makes the apparatus more complicated by retaining the tap and adding an arrangement to protect it. This was done by Brönsted (*loc. cit.*), who incorporated a device for letting in mercury above the tap, and by Palomaa and Salomon (*loc. cit.*), who similarly protected their stopper. However the protection thus given is not quite complete, and the applicability of the instrument remains limited: one must still consider the properties of the tap and the grease when planning experiments over a temperature range, and one must also exclude liquids which attack mercury (*e.g.*, nitric acid and halogens). The second method seeks to simplify the apparatus by abolishing the tap; and this is obviously the correct method, since it eliminates the leakage error completely, and widens the scope of the instrument to all liquid-phase reactions, and all temperatures, for which glass is not attacked. It has been applied by van 't Hoff (*Sitzungsber.*, 1910, **34**, 963) and by Benrath (*Z. anorg. Chem.*, 1926, **151**, 53). Van 't Hoff stoppered the capillary tube, evacuated the bulb through another tube, which he sealed, and then filled the dilatometer by removing the stopper under the surface of the experimental liquid. Benrath replaced the capillary tube by a tube so wide that the bulb could be filled through it. The former method is accurate but inconvenient and the latter convenient but inaccurate; we think we have advanced the technique by using tapless dilatometers which are both accurate and convenient.

The dilatometric method has not been used to the extent merited by its intrinsic scope and convenience, probably because of the restrictions imposed by taps and stoppers. The chief reactions hitherto studied are the aldol addition (Koelichen, Aberlof, Murphy; also Bell, J., 1937, 1637), keto-enol change (Wislicenus, *Chem. Z.*, 1904, 646; Göz, *Chem. Ztg.*, 1910, **33**, 1325), the mutarotation of sugars (Riiber, Brönsted), the reversible dimerisation of dihydroxyacetone (Bell and Baughan, J., 1937, 1947), hydrolysis of acetals (Brönsted, Palomaa and Salomon), hydrolysis of sucrose (Duane, Galeotti, Wright), the reversible hydrolysis of carboxylic esters (Galeotti, Benrath), the oxidation of sulphurous acid (Hoather and Goodeve), and various types of enzyme action (van 't Hoff, Galeotti, Sreenivasaya and Sestri, and Rona and Lemmer).

(c) *Previous Work on the Kinetics of Aromatic Nitration.*—The earliest recorded experiments on this subject are those of Spinola (*Annalen*, 1884, **224**, 283), who examined the nitration of benzene and some of its simpler derivatives with various amounts of nitric acid at various temperatures. No solvent was used, and hence the reaction mixtures were heterogeneous; no rate constants were obtained. The nitration of benzene in homogeneous conditions with nitrobenzene as the solvent was examined by Giersbach and Kessler (*Z. physikal. Chem.*, 1888, **2**, 676), and by Brauer (Diss., Heidelberg, 1899). Their main result was that the reaction started very rapidly and ended very slowly, so that all ordinary rate

coefficients, even third-order ones, decreased with time. The principal cause of this is undoubtedly the formed water, which ionises some of the unused nitric acid, so that it cannot enter into reaction. Holleman and de Bruyn (*Rec. Trav. chim.*, **1900**, **19**, 79) nitrated nitrobenzene in a large excess of the same substance, but obtained no recognisable reaction order.

The first to obtain velocity constants in the nitration of aromatic substances was Martinsen (*Z. physikal. Chem.*, 1904, **50**, 385; 1907, **59**, 605), who operated with nitric acid in sulphuric acid. Under these conditions the nitration of benzene was too rapid to be investigated, but that of nitrobenzene proved to be a straightforward second-order reaction. The same result was obtained for the nitration of a number of other compounds, such as 2 : 4-dinitrotoluene and the three nitrobenzoic acids; and it was again obtained much later by Klemenc and Schöller (*Z. anorg. Chem.*, 1924, **141**, 231) for the nitration of yet other compounds, such as 2 : 4-dinitro-*m*-xylene and the chloronitrobenzenes. The last-named authors made the significant observation that, in absolute sulphuric acid, dinitrogen pentoxide, if reckoned in the kinetic equation as $\frac{1}{2}(N_2O_5)$, gave the same second-order rate constants as nitric acid. This is further discussed in Section 10.

The rate of nitration of benzene and other compounds by means of nitric acid in acetic anhydride was first studied by Wibaut (*Rec. Trav. chim.*, 1915, **34**, 241), who obtained unsatisfactory evidence of a second-order law. Continuing the work, Cohen (*Proc. Acad. Sci. Amsterdam*, 1928, **31**, 692) showed that no such law obtained, that the nitration of benzene was catalysed by nitrous acid and was autocatalytic, and that side reactions proceeded by which the nitrating agent disappeared through interaction with the solvent. These results are confirmed in the latest work by Cohen and Wibaut (*Rec. Trav. chim.*, 1935, **54**, 409), in which the aromatic nitration was followed separately from the solvent reaction, and was concluded to be of the first order with respect to the benzene and of the third order with respect to nitric acid and nitrous acid collectively.

The nitration of phenol by nitric acid in water was first examined by Martinsen (*loc. cit.*), who showed that the reaction was autocatalysed by the nitrous acid produced. The same result was obtained by Klemenc (*Monatsh.*, 1914, **36**, 85; Klemenc and Ekl, *ibid.*, 1918, **39**, 641; Klemenc and Schöller, *loc. cit.*) with ether as solvent, and by Arnall (J., 1923, **123**, 3111) with alcohol. Klemenc and Ekl observed that the reaction in ether became very slow or stopped when the nitric acid was in excess of the phenol, a result which seemed contrary to the law of mass action, but can be explained by the formation of an unreactive oxonium salt. Klemenc and Schöller found that in the complete absence of nitrous acid nitration does not proceed; for water as solvent they gave the formula, rate $\propto [HNO_3]^{3 \cdot 2}[HNO_2]^{0 \cdot 3}$, and for ether, rate $\propto [HNO_3]^{2 \cdot 5}[HNO_2]^{0 \cdot 5}$.

Competitive nitration was unsuccessfully tried by Wibaut (*loc. cit.*). The only other published investigations along these lines are those of the present series (J., 1927, 2918; 1931, 1959; and the two preceding papers).

(2) *Dilatometric Methods.*

Most previous workers have established directly or indirectly that the distance, $l$, travelled by the meniscus of a dilatometer is accurately proportional to the amount by which the reaction under investigation has progressed. We have shown that the same is true for the nitrations quantitatively studied, all of which were accompanied by contractions. The formnla for the concentration of reactants at time, $t$, is thus $(l_\infty - l_t)D/R$. Here $D$, the fractional volume change per unit length travelled by the meniscus, is a constant of the dilatometer, and $R$, the fractional volume change per g.-mol. of reaction, is a constant for the reaction; $D$ was determined experimentally for each dilatometer, and $R$ for each reaction (Sections 2, b and 5, a).

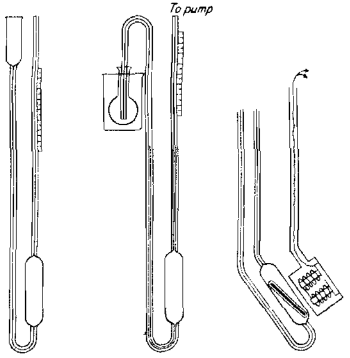
Preliminary experiments were carried out with dilatometers of a conventional design (type A) involving a tap, but consistent results could not thus be obtained. The recorded experiments were performed with tapless dilatometers (Section 2, a). Thermostats of considerable precision were necessary for use both above and below the room temperature (Section 2, c).

(a) *Design of Dilatometers*.—The principal designs are shown in Fig. 1. Instruments of type B were used for nitrations in which the concentration of aromatic compounds was in the range 0·1—0·5M. The bulb (10 c.c.) was made long and narrow in order to secure rapid heat exchange between the contents and the thermostat. The two limbs were of the same capillary tubing of bore 0·08 cm. Filling was accomplished through the funnel. Optical aid was provided by which the scale could be read to 0·01 cm.

The more sensitive instruments of type C were employed for more dilute solutions than those mentioned above. The lower part of each limb was made from wide capillary tubing, but the upper 15 cm. of each was made from the same length of capillary tubing of bore about 0·04 cm. Filling was accomplished by the aid of a small flask surrounded by liquid from the thermostat; one limb of the dilatometer dipped into this flask, whilst a vacuum pump was applied to the other.

A small modification, type BG, of the B-form of dilatometer was used in the longer experiments with more concentrated solutions, in order to eliminate the appreciable effect of evaporation on the behaviour of the meniscus. The funnel, instead of being sealed on, was

FIG. 1.




fitted with a ground joint. The funnel being detached, both capillary tubes terminated in male ground joints, and could thus be closed with ground caps, which were removed during reading.

Another modification, types BS and CS, permitted the stirring of the contents of these dilatometers. The bulb was inclined with its axis making an angle of 25° with the vertical direction, and 2" of 1/8" round malleable iron rod, enclosed in a pyrex glass tube, was included in the bulb when the instrument was being made. This stirring rod was actuated by an electromagnet, fed with interrupted direct current. The magnet was soldered into a brass case for immersion in the thermostat alongside the dilatometer, the electric leads passing out through a brass tube. The interrupter was of a simple brush-and-sector design, the sector-wheel being driven by a variable-speed motor. With this arrangement the speed of stirring could be varied between 25 and 250 strokes per minute.

(b) *Calibration of Dilatometers*.—The capillaries were calibrated by a method depending on the thermal expansion of a liquid. In almost every case, the corrections for variations of bore proved negligible, and it was in practice unnecessary to read more than one limb of the instrument: in other words, the dilatometer constant was the same for all parts of the single scale.

The dilatometer constants were determined by observation of the thermal expansion of conductivity water in an adjustable precision thermostat, a Beckmann thermometer being used for the measurement of temperature differences. Correction was made for the thermal expansion

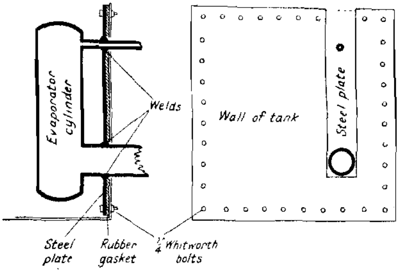
of the glass. The temperature correction for the dilatometer constant, calculated from the coefficient of expansion of the glass, was negligible.

(c) *Design of Thermostats.*—From the coefficient of expansion of nitromethane, the principal solvent used in the rate experiments, it was calculated that, for the most sensitive dilatometers, a temperature variation of 0·002° corresponded to a just perceptible displacement, 0·01 cm., of the meniscus. Temperature control was secured by means of two 20-gallon thermostats, one designed for use above the room temperature (25—80°), the other for use below (15° to −10°).

The former, built according to known principles, restricted temperature variation to less than 0·001°. The thermostat for low temperatures incorporated an adjustable permanent cooling unit, together with the usual low-powered intermittent heater. The cooling device was an "Electrolux, Type 100" unit, which has a heat abstracting power of $10^5$ cals./hour when working at its maximum input power of 300 watts. This type of refrigerator is very suitable for the purpose, because its rate of heat absorption depends only on the readily controlled input power to the heating element, provided that the flow of water through the condenser coils is above a necessary minimum.

The evaporator cylinder (cooling element) of the refrigerator unit was fitted into the cubical, copper tank of the thermostat as shown in Fig. 2. The tubes connecting the evaporator cylinder to the main body of the apparatus had been welded by the manufacturers through

FIG. 2.




an 18″ square steel plate. A slot was cut in one wall of the tank to accommodate these tubes, and the steel plate was bolted inside the wall, with an intervening rubber gasket, so that the evaporator cylinder was inside the tank and the rest of the refrigerator outside. The body of the refrigerator was bracketed to a heavy wooden base on which was built a platform to take the weight of the thermostat tank. This was set on a 2″ insulwood base, covered with a 2″ insulwood lid in two sections, and encased at the sides with 3½″ of insulwood and cork shavings. An efficient stirring system was installed, which consisted of a central shaft, with a propeller near the bottom and a turbine-fan near the top, together with a counter-shaft, run by a belt just below the lid, and operating a propeller in the corner shielded from the central stirrer by the evaporator cylinder. The liquid used to fill the tank was a mixture of water, ethylene glycol, and ethyl alcohol, which had a low viscosity and froze at −12°. The temperature variation in this thermostat did not exceed 0·002°.

### (3) *Analytical Methods.*

Two analytical methods, *viz.*, the estimation of nitrous acid and of aromatic nitroxyl, were employed to supplement the purely dilatometric measurements. Nitrous acid was estimated in each kinetic experiment. Aromatic nitroxyl was only occasionally measured, in order to provide an independent check on dilatometric determinations of the reaction constant, *R* (Section 2). We have made what appears to be a useful improvement in the Griess–Ilosvay method of estimating nitrous acid.

(a) *Colorimetric Estimation of Nitrous Acid.*—As nitrous acid has definite influence on the kinetics of the nitrations studied, it was important to be able to estimate it in the reaction

mixtures, *i.e.*, in the presence of large amounts of nitric acid and traces of various organic solvents and aromatic nitro-compounds. Only small quantities of solution being available, the methods of estimation were necessarily colorimetric.

The usual method for the colorimetric estimation of nitrous acid is the Griess–Ilosvay method (Lunge and Lwoff, *Z. angew. Chem.*, 1898, **7**, 348): an acetic acid solution of sulphanilic acid and α-naphthylamine produces by diazotisation and coupling the red colours to be compared, when it is treated, on the one hand, with the sample, and, on the other, with standard nitrite in sulphuric acid, both solutions being buffered with sodium acetate. This method could not be used for the nitration mixtures because these and the standard gave qualitatively different colours. They could be made comparable by omitting the sulphuric acid from the standard and the sodium acetate from both solutions, but the colours of the unbuffered solutions were unreliable, and the standard quantitatively unstable. Alternatively, the colours could be made qualitatively similar by adding sulphuric acid to the test solution, but the depth of colour was then not directly proportional to the nitrous acid concentration.

Zambelli has outlined a colorimetric method for the estimation of nitrous acid in water (J., 1887, **52**, 523): the nitrous acid is made to diazotise sulphanilic acid in acid solution, and the product is coupled with phenol or α-naphthol in ammoniacal solution. The following adaptation of this method gave results, where it was applicable, correct to 5%. A standard solution of sodium nitrite in 90% aqueous sulphuric acid was prepared which contained $10^{-6}$ g. of nitrogen per c.c.; 1% aqueous solutions of sulphuric acid and of α-naphthol were also made. The suitably diluted sample (1 c.c.), the sulphanilic acid solution (1 c.c.), aqueous sulphuric acid (1 c.c.), and water (10 c.c.) were mixed in a standard flask (25 c.c.), and after 10 minutes the α-naphthol solution (1 c.c.) was added, and the mixture made up to the mark with concentrated (*d* 0·880) aqueous ammonia. The standard nitrite solution (1 c.c.) was treated similarly to the sample, and the next day the colours were compared in a Klett colorimeter. This method was used in connexion with nitrations in which acetic anhydride was the solvent, but it could not be employed when the solvent was nitromethane because this produced a colour with ammonia.

For this reason a modification of the Griess–Ilosvay method was developed, which can be employed in the presence of nitromethane, and this proved extremely satisfactory. The main principle of the modification is to produce a colour from nitrous acid in acetic acid under fixed conditions, and to compare this with a standard solution of a stable dye of the same quality of colour, the dye solution having previously been matched against the colour produced from a solution of known nitrous acid content under the aforesaid fixed conditions. The details are as follows.

The reagent was prepared from sulphanilic acid and α-naphthylamine as recommended by Lunge and Lwoff (*loc. cit.*), and kept in full sealed tubes wrapped in black paper. The permanent colour standard was prepared by dissolving "SS-magenta (acid)" (from the British Drug Houses Ltd.) (0·2 g.) in water (2 l.) with a sufficient addition of hydrochloric acid, and diluting the solution 40-fold; it was kept in a well-stoppered bottle wrapped in black paper. A nitrite solution, the strongest of the series required, was prepared by dissolving 0·493 g. of sodium nitrite in 1 l. of water, sterilised by the addition of 5 c.c. of chloroform. This solution contained $10^{-3}$ g. of nitrogen per c.c., and portions of it were diluted to make other solutions of various smaller concentrations.

In order to standardise the dye solution, one of these nitrous acid solutions (1 c.c.), water (10 c.c.), the reagent solution (1 c.c.), and glacial acetic acid (5 c.c.) were successively introduced into a standard flask (25 c.c.), and the mixture was made up to the mark with water. After 25 minutes at room temperature, the colour was compared with that of the dye in a Klett colorimeter, and the ratio "nitrite colour"/"dye colour" was obtained. This was repeated for the whole range of nitrite concentrations, and the following results were obtained:

| | | | | | | |
|---|---|---|---|---|---|---|
| N as $HNO_2$ per c.c. ($10^{-6}$ g.) | 10·0 | 6·0 | 5·0 | 4·0 | 3·5 | 3·0 |
| Nitrite colour/dye colour | 7·47 | 4·50 | 3·85 | 3·05 | 2·75 | 2·34 |
| N as $HNO_2$ per c.c. ($10^{-6}$ g.) | 2·50 | 2·00 | 1·75 | 1·50 | 1·25 | 1·00 |
| Nitrite colour/dye colour | 2·06 | 1·59 | 1·43 | 1·23 | 0·89 | 0·71 |

From these figures a graph was constructed, which was not quite a straight line.

In order to carry out an estimation of nitrous acid, an experiment exactly like that just described is carried out (with the same pipettes, etc.), except that 1 c.c. of the suitably diluted sample is used in place of the 1 c.c. of a solution of known nitrous acid content. The colour ratio in conjunction with the graph determines the concentration of nitrous acid in the sample

With this method the maximum error was 4%, and we observed no interference from the organic materials contained in the samples.

(b) *Preparation of Nitric Acid free from Nitrous Acid.*—Here and elsewhere in this paper the term nitrous acid is taken to include any substances, such as certain oxides of nitrogen, which with water produce nitrous acid. On account of the effect of such substances on the kinetics of nitration it was important to have available nitric acid containing as little of them as possible. To this end, Kahlbaum's absolute nitric acid was twice distilled from admixture with 2 vols. of sulphuric acid, at 18 mm. in an all-glass still, the receiver of which was cooled in solid carbon dioxide. The crystalline product from the first distillation melted to a very pale yellow liquid, which was 99·9% acid, and contained about 0·2% of nitrous acid. The crystals from the second distillation melted to a colourless liquid which was absolute acid, and contained only a very small trace of nitrous acid. Such acid was either used at once, or stored for at most a few days in sealed tubes, which were wrapped in black paper and kept in a refrigerator at −5°. In order to avoid the small amount of decomposition arising from the heat of dilution which is liberated when the absolute acid is mixed with organic solvents, the nitric acid was weighed in solid state, and the solvent, cooled to just above its m. p., was poured on the crystals with shaking and in subdued light.

(c) *Estimation of Nitration Products.*—This type of auxiliary estimation was employed in order to prove that the cessation of a contraction as observed in a dilatometer corresponded to the completion of nitration, *i.e.*, that the total contraction corresponded to the introduction of one nitro-group per molecule nitrated. The interpretation of the dilatometry was checked in this way only for the nitrations in nitromethane, and in this case the aromatic nitro-compound was separated quantitatively from the solvent, and estimated by reduction with titanous chloride, exactly as described in the two preceding papers.

### (4) *Survey of the Properties of Solvents.*

The solvents examined may be divided into three groups which we term for convenience "slow," "intermediate," and "fast" solvents, the designations having reference to the rate of nitration of benzene. The classification is discussed in Section 10.

The progress of nitration was estimated partly dilatometrically, partly by titanometric determination of the aromatic nitro-compound, and partly by alkalimetric measurement of the nitric acid, these methods giving good agreement where they were used in order to check each other.

(a) *Slow Solvents.*—The examples examined were dioxan, acetic acid, and acetonitrile. In these solvents the nitration of benzene, and even of toluene, was very slow at temperatures of about 20—30°, even when the proportion and concentration of nitric acid were high. For example, 0·6% of nitration was found after a 1M-benzene solution in a mixture of equal weights of nitric acid and dioxan had been kept at 20·5° for 25 minutes. Only benzene derivatives with strongly activating groups, *e.g.*, anisole, were nitrated at readily observable rates with nitric acid in these solvents: dilatometric studies of such reactions will be reported later.

(b) *Intermediate Solvents.*—We found two solvents of this type, *viz.*, nitromethane and acetic anhydride.

With benzene and nitric acid, both in about 1M-concentration in nitromethane, nitration proceeded slowly at 30° and rapidly at 60°. Even at the latter temperature, however, the reaction stopped when about half the benzene had been nitrated: no velocity constants could be obtained, and all the usual types of "constant" diminished as reaction progressed. This is what Griersbach and others observed for nitration in nitrobenzene (Section I, c), and we explain it as already mentioned, *viz.*, by assuming that the water formed ionises the nitric acid and thus puts it out of action. Therefore, in the nitromethane experiments described in the followiug sections, we always employed a large excess of nitric acid, thus avoiding this disturbance. The usual orders of magnitude of the initial concentrations were 0·1M for the substance nitrated and 5M for the nitric acid. Under these conditions, benzene was nitrated, rather rapidly at room temperature, but at rates convenient for measurement at lower temperatures, *e.g.*, 0°. The solvent itself was not attacked by nitric acid, as was proved by keeping the materials together at 60° for one week in one of the sensitive dilatometers: the movement of the meniscus could not be read.

These observations directed our choice of nitromethane as the first solvent for detailed study.

It is well known that a solution of nitric acid in acetic anhydride contains an active nitrating agent, generally considered to be acetyl nitrate. We carried out a number of dilatometric experiments on nitration in an acetic anhydride solvent, but this was before Cohen and Wibaut's paper appeared (Section 1, c), and before our investigation (Part III, this vol., p. 905) into the by-products of nitration in acetic anhydride had been completed. We found dilatometrically, as Cohen and Wibaut did by analysis, that, in the nitration of benzene in acetic anhydride, the nitrating agent attacks the solvent as well as the benzene. After examining the dependence of the rates on nitrous acid and other factors, we came to the conclusion that the wanted and the unwanted reactions together formed a system too complicated for study by our method.

(c) *Fast Solvent.*—Sulphuric acid is a fast solvent. It is much too fast to permit the kinetic study of the nitration of benzene itself, or of any benzene derivatives except those containing strongly deactivating groups, such as nitroxyl. For such derivatives, however, the dilatometric method can be employed, and it is hoped later to report kinetic studies with this solvent.

## (Sections 5—8) Kinetics of Nitration in Nitromethane Solution.

### (5) *Kinetics of the Nitration of Benzene.*

For the reasons explained in Section 4, b we used always a very large excess of nitric acid, the active mass of which was therefore constant. The method of conducting the experiments was simply to mix two solutions, one of benzene in nitromethane and the other of nitric acid in nitromethane (Section 3, b), these solutions having previously been brought to the temperature of the thermostat; and then to introduce the mixture into the dilatometer already set up in the thermostat, and take a set of readings.

(a) *General Form of the Results.*—For all the experiments with benzene the curves expressing the dependence of the dilatometer reading on time had the form illustrated in Graph I (Fig. 3), which is the record of an experiment carried out at 0° in dilatometer B4. The unit of the ordinates, $l_\infty - l_t$, is 1 cm. of the scale of B4. The abscissæ are reckoned from the moment of mixing of the two solutions. No reading could be taken before 2 mins., which is but little longer than the time required to fill the dilatometer. After 50 mins. (in other experiments other periods, none less than 30 mins.) the readings remained constant indefinitely. The curves all fall sharply for 3 or 4 minutes, then exactly linearly for 30 minutes or longer, and then they suddenly become horizontal. We shall discuss in turn (i) the initial sharp fall, (ii) the total extent of fall, and (iii) the slope of the steady fall.

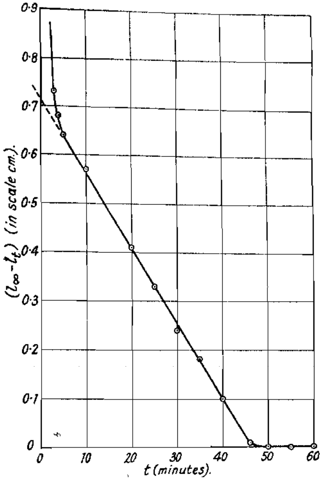
(i) We interpret this as a temperature disturbance, first because we expect one, and secondly because we have supporting evidence. Nitric acid has a positive heat of dilution with nitromethane, and hence, although the nitric acid and benzene solutions have the thermostat temperature before mixing, they must be warmer immediately after mixing. Furthermore, the mixed solutions must be warmed further during the filling of the dilatometer by passage through those parts of it which project outside the thermostat. Hence we expect an initial disturbance due to the cooling of the solution in the dilatometer to the thermostat temperature. Evidence that this is the cause of the initial sharp contraction is given in Section 5, b. Therefore in considering the progress of nitration we disregard the initial contraction, and treat the graph representing the volume change due to nitration as a straight line throughout its length. The straight part of each time graph was produced back as shown in Fig. 3, the intercept on the axis of ordinates being taken as corresponding to the volume of the solution at zero time and at thermostat temperature.

(ii) The total fall in $l_\infty - l_t$, counting from the extrapolated value for $t = 0$, was multiplied by the dilatometer constant ($D = 0{\cdot}00129$ for B4) and thus converted into a fractional contraction. In Table I, fractional contractions (col. 3) are compared with initial benzene concentrations (col. 2). Col. 4 contains the fractional contractions per unit molar initial concentration of benzene ($R$), and it will be seen that these values are substantially constant. (These experiments were done in ice-water. The low-temperature thermostat, which was

built soon afterwards, gave a great improvement in accuracy.) The constancy shows that the total contraction, reckoned as described, corresponds to the introduction of a constant number of nitroxyl groups per benzene molecule. The following experiments show that this number is one.

An experiment of the same type was carried out except that nitrobenzene was used in place of benzene. After 4 hours in the dilatometer at 0° there was still no contraction that could be read on the scale. This shows that dinitration could not have participated in the experiments with benzene, none of which lasted as long as 4 hours at 0°.

Fig. 3.




*Graph I.*

*General Form of Results (as shown by Expt.* 191).

A more direct confirmation was obtained by keeping a benzene reaction mixture in the thermostat at 0° for a somewhat longer time than a similar mixture in a dilatometer would have needed to cease contracting, and then estimating the aromatic nitroxyl by reduction with titanous chloride (Section 3, c). The number of nitroxyl groups per benzene molecule was estimated as 1·003, *i.e.*, unity to within the error of measurement.

(iii) The rectilinear character of those parts of the graphs which represent nitration shows that the nitration is a reaction of order zero with respect to the substance nitrated. The gradients of the graphs (cm. min.$^{-1}$) can be converted into zero-order rate constants, $k_0$ (sec.$^{-1}$ g.-mol. l.$^{-1}$), by multiplication by $D/60R$. These rate constants were at first not reproducible and seemed to bear no relation to the initial concentration of nitric acid; but they became reproducible when the same specimen of nitric acid was used in the same concentration. This is illustrated in the last three cols. of Table I: after seven experiments with various samples of nitric acid, two pairs were carried out, one pair with the same sample of freshly distilled acid, and the other with the same sample of Kahlbaum's acid. Since the main difference between these two types of acid is that the former contains little, and the latter much, real or potential nitrous acid (lower oxides of nitrogen), it appears that such substances are anticatalytic.

TABLE I.

| Expt. No. | Benzene concn. (M). | Fractional contrn. | Contrn. per g.-mol. $C_6H_6$. | Nitric acid. Sample.* | Concn. (M). | $10^3 k_0$. |
|---|---|---|---|---|---|---|
| 62 | 0·563 | 0·00798 | 0·0139 | — | 6·14 | 6·04 |
| 63 | 0·390 | 0·00534 | 0·0137 | — | 6·20 | 7·86 |
| 64 | 0·303 | 0·00406 | 0·0134 | — | 6·55 | 7·07 |
| 65 | 0·198 | 0·00268 | 0·0135 | — | 6·55 | 8·61 |
| 71 | 0·290 | 0·00369 | 0·0127 | — | 6·27 | 6·07 |
| 73 | 0·443 | 0·00566 | 0·0128 | — | 7·00 | 11·19 |
| 79 | 0·299 | 0·00406 | 0·0136 | — | 6·11 | 6·53 |
| 98 | 0·414 | 0·00558 | 0·0135 | D | 6·30 | 11·92 |
| 99 | 0·414 | 0·00524 | 0·0127 | K | 6·30 | 4·21 |
| 100 | 0·414 | 0·00567 | 0·0137 | D | 6·30 | 11·16 |
| 101 | 0·414 | 0·00535 | 0·0129 | K | 6·30 | 4·32 |

Mean reaction constant ($R$) = 0·0133.

* D = Sample of distilled acid. K = Sample of Kahlbaum's acid (undistilled).

(b) *Test for Rate-controlling Physical Process.*—It was necessary to determine whether the zero-order rates were determined by a rate of transport. This was investigated as follows. The same reaction mixture was simultaneously introduced into two dilatometers, one of which was furnished with stirring gear (Section 2, a). They were set side by side in the thermostat, and, while the mixture in one was stirred, the contraction in each was observed. The results were as follows.

For the first 4 minutes from the time of making the mixture, the behaviour observed in the two dilatometers differed widely: the unstirred solution showed the usual sharp initial contraction, but the stirred mixture did not. This confirms our view (Section 5, a) that the sharp initial contraction is a thermal effect: by stirring we bring the reaction mixture into temperature equilibrium with the thermostat before the first reading can be taken, and thus the whole of the observed contraction is linear.

For the remainder of the period of contraction, this process followed the same linear course in both dilatometers; also it proceeded at the same rate and ceased at the same moment in the stirred and unstirred solutions. This shows that the observed rate is not conditioned by a rate of transport, if we except heat transport during the first few minutes.

(c) *Test for Rate-controlling Heterogeneous Reaction.*—Next it was necessary to test for a surface reaction, and to this end a dilatometer (B 16) was prepared which had its internal glass surface artificially increased by the inclusion of glass powder. The glass particles had been graded and some of them measured: from the measurements it was computed that the internal surface area was 12·5 times that of a similar dilatometer having no glass powder. The same reaction mixture was introduced into the empty and into the glass-filled dilatometer, which were set side by side in the thermostat. In both, the contractions followed the same linear course, proceeded at the same rate, and terminated at the same moment. This was found true for the whole range of rates encountered in the subsequent investigation (Sections 5, d and 5, e). It follows that the zero-order rates are not controlled by a surface reaction.

(d) *Effect of "Nitrous Acid."*—References to the amount or concentration of nitrous acid will be understood to refer to the nitrous acid equivalent of those substances which yield nitrous acid on dilution of the reaction mixtures with water.

(i) *Method of experiment.* In this group of experiments the nitric acid concentration and temperature were kept constant, the former being 5M and the latter 0°. Since it had been established that the rates are independent of the benzene concentration, this concentration was not accurately standardised; it was always about 0·1M. The nitrous acid concentration was varied. A 5M-solution of vacuum-distilled nitric acid in nitromethane was made up, with the precautions against decomposition mentioned in Section 3, b. A similar solution was made from nitric acid rich in nitrous acid. By mixing these solutions in various proportions it was possible to obtain solutions containing the same concentration of nitric acid but different amounts of nitrous acid. To each solution (15 c.c.) the benzene was added (5 drops), and part was introduced into a dilatometer, whilst

another part was diluted with water (50—500 vols.) to give a solution suitable for the estimation of nitrous acid (Section 3, a).

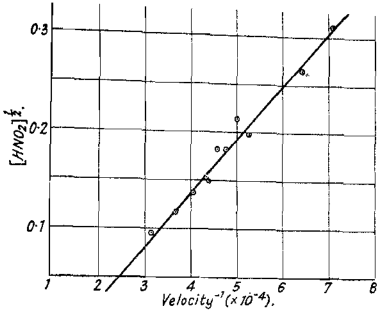
(ii) *Constancy of nitrous acid.* In four experiments the nitrous acid was estimated at the beginning and also at the end of the contraction period. The results were as follows:

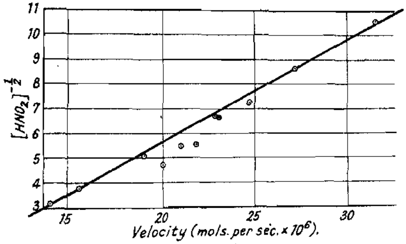
| | | | | |
|---|---|---|---|---|
| Initial [$HNO_2$] (M) .......................... | 0·0861 | 0·0760 | 0·0545 | 0·0211 |
| Final [$HNO_2$] (M) .......................... | 0·0832 | 0·0768 | 0·0563 | 0·0214 |

The agreement of the initial and the final concentration in each experiment being within the error of the determination (Section 3, a), it follows that nitrous acid is not appreciably consumed or produced during nitration. Having established this, we subsequently measured only initial nitrous acid concentrations.

FIG. 4.

*Graph II.*




*Graph III.*

(iii) *Functional connexion with rate.* Eleven further experiments (a "block") were carried out with nitrous acid concentrations ranging from less than 0·01M to 0·1M. The zero-order rate constants are given in Table II (Expts. 188—199; [$HNO_3$] = 5M). By an examination of these figures, two simple relationships can be suggested between the nitrous acid concentration and the rate of reaction:

(α) The square root of the nitrous acid concentration is a linear function of the reciprocal velocity, as shown in Graph II (Fig. 4): $1/k = a + b[HNO_2]^{1/2}$.

(β) The reciprocal square root of the nitrous acid concentration is a linear function of the velocity, as shown in Graph III (Fig. 4): $k = a' + b'/[HNO_2]^{1/2}$.

These relations are, of course, not equivalent. The former seems slightly preferable on experimental grounds (see graphs), and we can interpret it theoretically (Section 9, a).

(e) *Effect of Nitric Acid.*—Several blocks of experiments were carried out, each quite similar to the block of eleven just described. The temperature was 0° throughout. In each block the nitric acid concentration was kept constant, and the rate of nitration was traced as a function of the nitrous acid concentration. From one block to the next the nitric acid concentration was changed in steps of ½M over the range 3M to 7M. Beyond these limits the rates were of inconvenient orders of magnitude, and the accuracy correspondingly diminished. The rate constants (sec.$^{-1}$ g.-mol. l.$^{-1}$) are given in Table II.

TABLE II.

*Zero-order Rate Constants for the Nitration of Benzene at 0°.*

| Expt. No. | $[HNO_2]$, (M). | $10^6 k_0$. |
|---|---|---|
| $[HNO_3]$ = 7·0M. | | |
| 294 | 0·0083 | 184·2 |
| 296 | 0·0321 | 98·5 |
| 297 | 0·0516 | 88·0 |
| 299 | 0·113 | 71·9 |
| 298 | 0·125 | 65·7 |
| 295 | 0·150 | 58·1 |
| $[HNO_3]$ = 6·5M. | | |
| 288 | 0·0073 | 103·0 |
| 290 | 0·0212 | 77·0 |
| 291 | 0·0373 | 64·3 |
| 293 | 0·0822 | 51·3 |
| 292 | 0·119 | 44·6 |
| 289 | 0·133 | 42·3 |
| $[HNO_3]$ = 6·0M. | | |
| 236 | 0·0226 | 55·5 |
| 235 | 0·0472 | 46·8 |
| 237 | 0·0564 | 42·5 |
| 234 | 0·0674 | 38·2 |
| 232 | 0·104 | 33·5 |
| 231 | 0·118 | 31·2 |

| Expt. No. | $[HNO_2]$, (M). | $10^6 k_0$. |
|---|---|---|
| $[HNO_3]$ = 5·5M. | | |
| 239 | 0·0138 | 35·8 |
| 240 | 0·0513 | 26·2 |
| 241 | 0·0715 | 24·3 |
| 245 | 0·0860 | 24·2 |
| 242 | 0·0788 | 23·0 |
| 244 | 0·101 | 22·3 |
| 243 | 0·128 | 20·5 |
| $[HNO_3]$ = 5·0M. | | |
| 188 | 0·0089 | 32·8 |
| 190 | 0·0134 | 27·2 |
| 191 | 0·0189 | 24·7 |
| 193 | 0·0225 | 22·9 |
| 192 | 0·0228 | 23·0 |
| 199 | 0·0330 | 21·8 |
| 197 | 0·0331 | 21·0 |
| 198 | 0·0392 | 19·0 |
| 196 | 0·0455 | 20·0 |
| 195 | 0·0702 | 15·6 |
| 194 | 0·0984 | 14·1 |

| Expt. No. | $[HNO_2]$, (M). | $10^6 k_0$. |
|---|---|---|
| $[HNO_3]$ = 4·5M. | | |
| 262 | 0·0062 | 13·3 |
| 258 | 0·0081 | 16·1 |
| 259 | 0·0089 | 13·3 |
| 264 | 0·0089 | 13·2 |
| 265 | 0·0116 | 12·3 |
| 261 | 0·0139 | 13·3 |
| 267 | 0·0258 | 10·7 |
| 268 | 0·0402 | 9·60 |
| 266 | 0·0883 | 8·01 |
| 260 | 0·0896 | 7·88 |
| 263 | 0·0947 | 7·43 |

| Expt. No. | $[HNO_2]$, (M). | $10^6 k_0$. |
|---|---|---|
| $[HNO_3]$ = 4·0M. | | |
| 270 | 0·0056 | 8·45 |
| 271 | 0·0115 | 7·35 |
| 272 | 0·0190 | 6·63 |
| 273 | 0·0356 | 6·05 |
| 269 | 0·0764 | 4·63 |
| $[HNO_3]$ = 3·5M. | | |
| 274 | 0·0041 | 4·73 |
| 276 | 0·0093 | 4·13 |
| 277 | 0·0140 | 3·86 |
| 278 | 0·0335 | 3·32 |
| 279 | 0·0799 | 3·02 |
| 275 | 0·0803 | 2·70 |
| $[HNO_3]$ = 3·0M. | | |
| 283 | 0·0046 | 3·52 |
| 286 | 0·0347 | 1·99 |
| 282 | 0·0575 | 1·64 |

Each block of experiments obeyed the relationship $k_0^{-1} = a + b\,[HNO_2]^{1/2}$, but the parameters $a$ and $b$ varied from one block to another. The graphs (IV and V) from which $a$ and $b$ were computed as functions of the nitric acid concentration are shown in Figs. 5 and 6. The values thus obtained are in Table III.

TABLE III.

*Parameters of the Equation* $k_0^{-1} = a + b[HNO_2]^{1/2}$.

| $[HNO_3]$ | 7·0 | 6·5 | 6·0 | 5·5 | 5·0 | 4·5 | 4·0 | 3·5 | 3·0 |
|---|---|---|---|---|---|---|---|---|---|
| $10^{-4}\,a$ | 0·35 | 0·56 | 0·74 | 1·74 | 1·74 | 5·0 | 8·3 | 17·2 | 15·7 |
| $10^{-4}\,b$ | 3·30 | 4·85 | 7·03 | 8·80 | 17·3 | 27·0 | 47·5 | 70·0 | 188·5 |

The dependence of the parameters $a$ and $b$ on the nitric acid concentration (represented by $N$) is shown in graphs VI and VII (Fig. 7). It will be seen that the plot of $1/a$ against $N^6(27 - N)$, and the plot of $1/b$ against $N^5(27 - N)$, are both straight lines which pass through the origins of the co-ordinates.

The whole set of results can thus be represented by the equations

$$k_0^{-1} = a + bn^{1/2} \qquad (1)$$

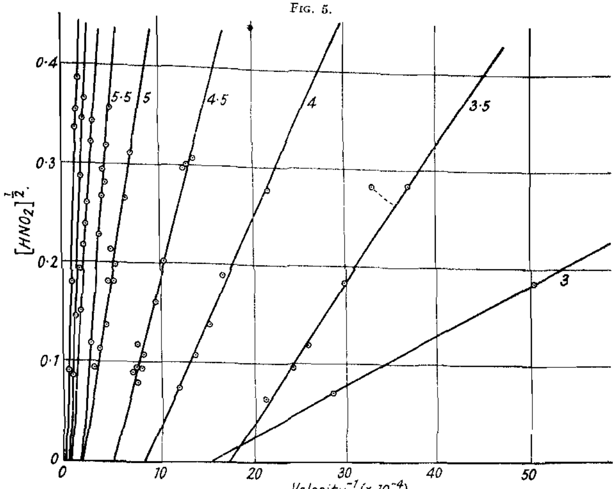
$$a = AN^{-6}(27 - N)^{-1} \qquad (2)$$

$$b = BN^{-5}(27 - N)^{-1} \qquad (3)$$

where $n$ denotes the nitrous acid concentration. Equation (1) has theoretical significance, but, owing to the large concentrations of nitric acid, equations (2) and (3) cannot be other than semi-empirical functions of concentration; the quantity $27 - N$ represents the concentration of the solvent. The constants $A$ and $B$ depend only on temperature, and for 0° the values are

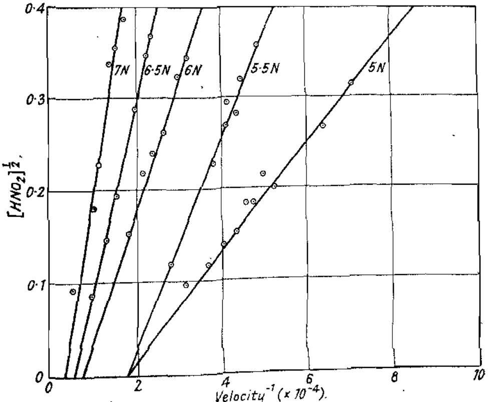
$$A = 8{\cdot}4 \times 10^9 \qquad B = 11{\cdot}3 \times 10^9$$

FIG. 5.




*Graph IV.*
*Blocks of Nitrations in* 7N- *to* 3N-HNO$_3$ *solution—in steps of* 0·5N *from left to right.*

FIG. 6.



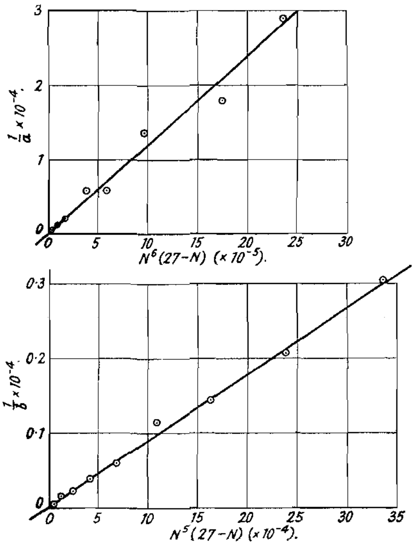

*Graph V.*
*Block of Nitrations in* 7N- *to* 5N-HNO$_3$ *solution.* (*Five times scale of IV.*)

(f) *Effect of Temperature.*—This has not been fully investigated, because we cannot, as is obvious from the reaction order, deduce the activation energy for any reaction directly affecting the aromatic compound.

Experiments at temperatures other than 0° were carried out for two nitric acid concentrations, $N = 3{\cdot}0$ and $5{\cdot}0$ M; the former concentration was investigated at 20° and the latter at $-10°$ and 10°. As before, several blocks of experiments each corresponding to a particular temperature and nitric acid concentration were carried out, and within each block the nitrous acid concentration was varied. The whole series of experiments gave rectilinear reaction–time curves, and all the blocks of experiments gave straight-line

Fig. 7.

*Graph VI.*




*Graph VII.*

curves when the reciprocals of the zero-order rate constants were plotted against the square roots of the nitrous acid concentrations. The whole set of results can thus be summarised in terms of the dependence of the parameters $a$ and $b$ of equation (1) on temperature and nitric acid concentration. This is done in Table IV. From these results we can deduce the factors by which $a$ and $b$ decrease for a rise of temperature of 10°, at temperatures not too far removed from 0°: these factors are given in the last line but one in the table. Since, both for $a$ and for $b$, the temperature factors are substantially independent of the nitric acid concentration, their mean values, given in the last line of the table, may be accepted as the factors by which the constants $A$ and $B$ of equations (2) and (3) respectively become decreased for a rise of 10° in temperature. Putting the same statement into a logarithmic form we can set up equations (4) and (5) which, with (1), (2), and (3), compactly

express the kinetics of the reaction over the range of variables investigated (θ, −10° to +20°; *N*, 3·0—7·0M; *n*, 0·005—0·15M; $[C_6H_6]$, <0·01 to 0·5M):

$$\log_{10} A = 9{\cdot}924 - 0{\cdot}0415\theta \qquad (4)$$

$$\log_{10} B = 10{\cdot}053 - 0{\cdot}0544\theta \qquad (5)$$

TABLE IV.

*Temperature Variation of Parameters of Equations* (1), (2), *and* (3).

| Temp. | $N$ = 3·0M. | | $N$ = 5·0M. | |
|---|---|---|---|---|
| | $10^{-4}a$. | $10^{-4}b$. | $10^{-4}a$. | $10^{-4}b$. |
| −10° | — | — | — | 5·70 |
| 0 | 15·7 | 189 | 1·52 | 1·80 |
| +10 | — | — | 0·60 | 0·48 |
| +20 | 2·15 | 15·2 | — | — |
| Factors by which *a* and *b* fall for 10° rise of temperature | 2·7 | 3·5 | 2·5 | 3·6 |
| Factors by which *A* and *B* fall for 10° rise of temperature | *A*, 2·6 | | *B*, 3·5 | |

Let us assume that *A* and *B* each satisfy an equation of the Arrhenius type: $A = B_A e^{-E_A/RT}$ and $B = B_B e^{-E_B/RT}$. We can then estimate $E_A$ and $E_B$:

$$E_A = -15 \text{ kilocals.}; \quad E_B = -19 \text{ kilocals.}$$

The significance of $E_A$ and $E_B$ is considered in Section 9, a.

### (6) *Kinetics of Nitration of Toluene and Ethylbenzene.*

We shall summarise these experiments very briefly, because it will appear that all the results for toluene and ethylbenzene can be reduced to one simple statement. As before, we employed temperatures in the neighbourhood of 0° and solutions containing large, time-invariant concentrations of nitric acid.

(a) *General Form of the Results.*—The contraction–time curves for toluene and ethylbenzene were of exactly the same form as those previously obtained for benzene (see Section 5, a). This was true over the range of variables considered in the case of benzene.

(b) *The Absolute Rates.*—Since the rates of nitration of benzene, toluene, and ethylbenzene are independent of the concentration of hydrocarbon, we should expect them to be independent of which hydrocarbon is being nitrated. This deduction was tested in experiments of which the following is typical.

A solution of nitric acid (4·00M) in nitromethane, known as to its content of nitrous acid (0·0731M), was divided into three portions, which were treated severally with benzene, toluene, and ethylbenzene in quantities sufficient to make solutions about 0·1—0·2M with respect to the hydrocarbons. Using C-type dilatometers, the contractions were followed at 0°, and the zero-order rate constants calculated as usual. The rates (× $10^5$) were: benzene, 527; toluene, 530; ethylbenzene, 532 $\text{sec.}^{-1}$ g.-mol. $\text{l.}^{-1}$; that is, they were equal to within the error of observation. This result was generalised by means of similar experiments for other nitric and nitrous acid concentrations and temperatures within the range of variation already illustrated.

Therefore, the zero-order rates of nitration of toluene and ethylbenzene are quantitatively defined by the equations (1—5) already given for the rate of nitration of benzene.

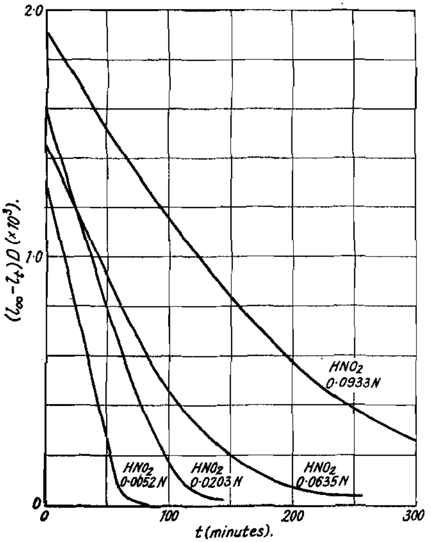
### (7) *Kinetics of the Nitration of Fluoro-, Chloro-, Bromo-, and Iodo-benzene (Qualitative Features).*

Unlike the nitration of benzene and its monoalkyl derivatives, nitration of the monohalogeno-derivatives of benzene followed no simple order. For this reason, we are unable, on the basis of the relatively few experiments so far performed, to give exact mathematical expression to the results. We shall therefore illustrate the latter by means of typical curves, and generalise only with respect to qualitative features. It is probable that with the help of many more experiments (several hundreds) we could set down the rate

equations complete with their numerical parameters, as has been done for the simpler kinetics of the hydrocarbons; this follows because even the qualitative features, as elucidated in the present work on the halogeno-compounds, are sufficiently significant in relation to the results for hydrocarbons to indicate the general form which the rate laws must assume (cf. Section 9, c).

As before we have worked with large, time-invariant concentrations of nitric acid, which were changed from one block of experiments to another, and with concentrations of nitrous acid which were varied within each block. All the experiments of this series were, however, done at 0°.

FIG. 8.




*Graph VIII.*

*Nitration of Fluorobenzene in 5N-Nitric Acid at 0°.*

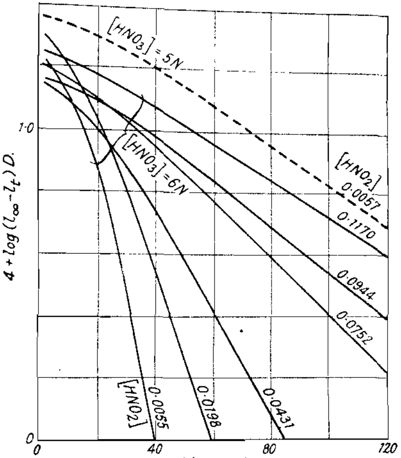
(a) *General Comparison with Benzene.*—There were two qualitative differences between the behaviour of the halogenobenzenes, on the one hand, and benzene, toluene, and ethylbenzene, on the other. The first was that the volume changes observed with the halogenobenzenes were all considerably slower than with the hydrocarbons under the same conditions. Unlike the hydrocarbons, the halogenobenzenes showed individual differences, but the above statement is true of all of them. The point is illustrated in Fig. 10, in which the reaction–time curves of the four halogenobenzenes are compared with one another and with curves for benzene, for the same temperature and nitric and nitrous acid concentrations.

The second difference was that the volume–time graphs for the halogenobenzenes, instead of being rectilinear as for the hydrocarbons, were markedly curved, being convex to the time axis. This is illustrated in Figs. 8 and 10 (lower part), and it means that the rate of reaction has some dependence on the concentration of the substance which is being

nitrated. The rate, being sensitive to the concentration, must be sensitive also to the chemical nature of the substance nitrated, and hence it is consistent that the halogeno-benzenes do not all behave alike, as the hydrocarbons do.

There were also two qualitative similarities between the behaviour of the halogeno-benzenes and that of the hydrocarbons. One was that nitrous acid was an anticatalyst, with the same order of rate-diminishing power for the halogenobenzenes as for the hydrocarbons. This is illustrated by the four curves in Fig. 8, which relates to the nitration of fluorobenzene at 0° in a 5M-nitric acid solution containing various proportions of nitrous acid. It will be appreciated that no special significance attaches to the crossing of curves such as those shown in Figs. 8, 9, and 10 : each graph starts from a point determined by the amount of the aromatic substance taken for nitration, and hence a curve for a faster

Fig. 9.




*Graph IX.*

*Nitration of chlorobenzene at* 0°.

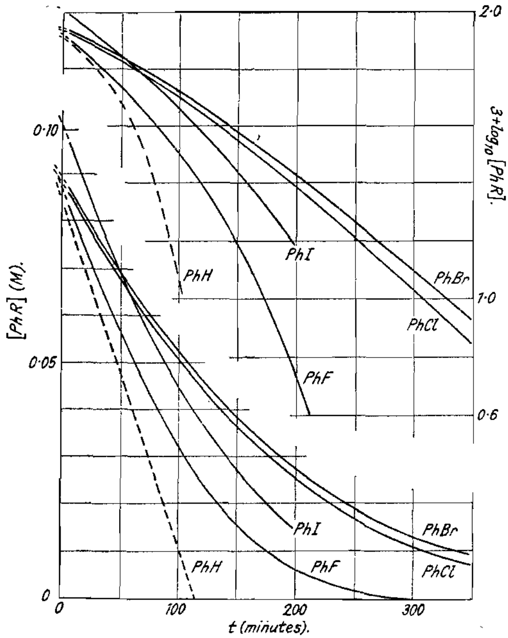
reaction with more material may cut one representing a slower reaction with less. The important point is that the slopes of the graphs in Fig. 8 diminish with increasing concentration of nitrous acid, provided we compare slopes at corresponding stages of contraction. The same point is illustrated by the full-lines curves of Fig. 9, which relates to the nitration of chlorobenzene at 0° in 6M-nitric acid solutions containing various concentrations of nitrous acid : the method of plotting is different, but the relative rates can be assessed by an analogous comparison of slopes.

The second point of similarity relates to the effect of the concentration of nitric acid on the speed. As for the hydrocarbons, so also for the halogeno-compounds, the speed increases very rapidly with increase in the nitric acid concentration within the investigated range. In Fig. 9, along with the curves for the block of experiments on the nitration of chlorobenzene at 0° in 6M-nitric acid, we include the curve for one experiment of a similar block in 5M-nitric acid. This curve (broken line) may be compared with the lowest curve in the same diagram, since the nitrous acid concentrations for the two are practically the

same. The large difference of slope is due to the moderate difference of nitric acid concentration.

(b) *Form of the Volume-time Curves.*—The convexity of these curves to the time axis may be expressed formally by the statement that the effective reaction order with respect to the aromatic substance is greater than zero. The effective reaction order is smallest in the examples of fluoro- and iodo-benzene. In the contraction–time curves for these compounds, *e.g.*, those reproduced in Fig. 8, one can see distinct vestiges of the rectilinear law which obtains for benzene itself.

FIG. 10.




*Graph X.*

*Comparative nitrations of benzene and the halogenobenzenes.*

The effective reaction order is greatest for chloro- and bromo-benzene, but even for these substances it is not as great as unity. This is illustrated in Fig. 9, where, instead of plotting the contraction $[(l_\infty - l_t)D]$ itself, we have plotted its logarithm, against the time. If the reaction order with respect to the chlorobenzene were unity, these curves would be straight lines: their concavity to the time axis shows that the effective reaction order is less than unity.

Further inspection of Fig. 8 shows that the effective reaction order is far from being constant throughout a single experiment: the volume–time graphs are considerably less curved at the beginning than in the later stages of contraction. This means that the rate

of nitration becomes more and more dependent on the substance nitrated the less there is of it. The same thing is shown in another way in Fig. 9, from which it can be seen that the logarithmic curves are rather strongly bent initially, and become more nearly straight towards the end of reaction. This signifies that the effective reaction order, although well below unity at the commencement of reaction, rises towards unity as nitration proceeds. Further illustrations will be seen in the curves of Fig. 10.*

(c) *Comparison of Rates for the Four Halogenobenzenes.*—Comparison can be effected by interpolation to identical conditions but the direct method, previously used for benzene, toluene, and ethylbenzene, has also been employed. The following is an example.

A solution of nitric acid (5·00M) in nitromethane, known as to its content of nitrous acid (0·115M), was divided into five portions, which were severally treated with benzene and with fluoro-, chloro-, bromo-, and iodo-benzene, in quantities sufficient to form solutions approximately 0·1M with respect to the several aromatic compounds. C-Type dilatometers being used, the contractions were followed at 0°. The results are shown graphically in Fig. 10.

Similar experiments were carried out with other concentrations of nitric and nitrous acids. Although the absolute rates changed very greatly with changes in the concentration of these reagents, the following comparative statements hold true for all experiments. (1) The compounds fall into three groups with regard to rate of nitration: fluoro- and iodo-benzene nitrate at nearly the same rate, which is smaller than the rate for benzene; and chloro- and bromo-benzene also nitrate at about the same rate, which is smaller than for the other compounds: PhH > PhF,PhI > PhCl,PhBr. The slight distinction between chloro- and bromo-benzene is in the direction PhCl > PhBr.† (2) The compounds divide themselves into the same three groups with respect to the dependence of the reaction rate on the concentration of the substance nitrated. With benzene there is no dependence. With fluoro- and iodo-benzene there is a small dependence in the initial stages, rising to a considerable dependence in the later stages, of reaction. With chloro- and bromo-benzene there is considerable dependence in the initial stages, and this rises nearly to proportionality as reaction proceeds.

It will be observed that there is a general antiparallelism between the rate of nitration of the aromatic substance under given conditions and the dependence of the rate on the concentration of the aromatic substance; and, when, as in benzene and the alkylbenzenes, the rate has reached a value which apparently cannot be exceeded, its dependence on the concentration has vanished.

## (8) *The Colour accompanying Nitration.*

The production of red colours in the course of the nitration of aromatic substances by means of nitric acid in nitromethane (and in acetonitrile) was first reported in Part II (J., 1931, 1966). These colours arise whilst nitration is actually in progress; they fade as the reaction comes to a natural end, but can be destroyed at any moment by the addition of water (which also stops nitration). On acconnt of their apparent connexion with the nitration process, we have investigated these colours both qualitatively and colorimetrically.

(a) *Observations on the Colours arising in Nitration.*—The colours initially produced by adding equivalent quantities of different aromatic compounds to equal portions of the same solution of nitric acid in nitromethane at the same temperature differ considerably. The rule is that, *ceteris paribus*, the more intense colours are given by those aromatic compounds that are more reactive in electrophilic substitution; *e.g.*, the compounds that would have the higher rates of nitration as determined in competitive experiments. Thus the colour intensity increases in the series PhCl < PhH < PhMe < *p*-$Me_2C_6H_4$; and, although the colours are similar enough in quality to be matched in a colorimeter, the direct visual impression given by solutions of comparable concentration may range in such a series from pale yellow in chlorobenzene, through orange-red and blood-red, almost to black in *p*-xylene.

* The crystallisation of *p*-iodonitrobenzene occasionally interfered with the investigation of the latter part of the reaction of iodobenzene.

† These results are consistent with the competition investigation of Part IV, where the rate series PhF ≫ PhCl > PhBr ≪ PhI was found (preceding paper).

The colours initially produced by adding different quantities of the same aromatic compound, *e.g.*, benzene, to equal portions of the same solution of nitric acid in nitromethane at the same temperature are more intense the greater the quantity of the aromatic compound. As the colours at once begin to fade, no attempt was made to establish the relation between initial colour and initial concentration quantitatively. The rate of fading was, however, measured colorimetrically in the case of benzene, the method being to match the fading solution against diminishing lengths of a column of alcoholic iodine. The colour intensity was found to fall linearly with time to within the accuracy of the measurements; and the time required for the total fall was equivalent to the time required to complete nitration. Since we know from the work described in Section 5 that the concentration of benzene falls linearly with time during nitration, the conclusion must be drawn that the colour intensity is directly proportional to the benzene concentration in any given nitration solution at constant temperature.

The addition of equal quantities of the same aromatic compound, *e.g.*, benzene, to equal amounts of solutions in nitromethane containing identical concentrations of nitric acid but varying concentrations of real or potential nitrous acid, at the same temperature, produced initial colours increasing in intensity as the nitrous acid concentration increased. The addition of urea inhibited the formation of colours.

The addition of equal amounts of benzene to equal portions of the same solution of nitric acid (containing nitrous acid) in nitromethane at different temperatures produced initial colours having greater intensity the lower the temperature.

(b) *Production of the Colours by Various Reagents.*—The colours produced in the experiments mentioned below, which were carried out with benzene, could be visually matched against the colours arising in nitration solutions.

A number of observations were made with oxides of nitrogen. When nitric oxide was passed through a nitration solution the depth of colour at first increased, but the nitric acid was decomposed, nitrogen peroxide being formed. This experiment was then varied by omitting various substances or replacing them with others. When the nitric acid was omitted there was no colour; but when, in place of nitric acid, a little sulphuric acid or phosphoric oxide was added the usual colour was generated, in the former case homogeneously and in the latter on the surface of the oxide. The omission of nitromethane made no difference to any of these observations. When the benzene was omitted no colour was formed in any circumstances. When all these experiments, except those involving nitric acid, were repeated using dinitrogen trioxide, and again using nitrogen dioxide, in place of nitric oxide, the results were exactly the same.

(c) *Relation of Colour to Nitration Kinetics.*—The above observations establish that a coloured complex is formed from benzene and a lower oxide of nitrogen in the presence of an anhydrous condensing agent such as sulphuric or nitric acid or phosphoric oxide; and, furthermore, that the complex is in mobile equilibrium with its factors; and that it is on the low-energy side of a mobile equilibrium.

The same observations also establish that the formation of the coloured complex plays no essential rôle in the mechanism that determines the reaction kinetics. This follows because the colour intensity is proportional to the benzene concentration, whilst the nitration rate is independent of this concentration, wherefore the colour intensity can have no connexion with the rate. It is nevertheless true that real or potential nitrous acid is concerned both in the formation of the colour and in the determination of the rate. We conclude that the coloured substance is produced in such small quantity that the consumption of nitrous acid in its formation is negligible: were this not so, the liberation of nitrous acid due to the progressive reversal of complex formation as colour fades in the course of nitration would, by reason of the anticatalytic effect of nitrous acid, give rise to a progressively growing deceleration of the reaction; whereas, in fact, the velocity remains constant. This holds for benzene, toluene, and ethylbenzene, although it may not hold for hydrocarbons, such as *p*-xylene, which give considerably more intense colours and non-linear reaction-time curves. We do not further discuss such cases in this paper, as much more detailed investigation of them seems to be required.

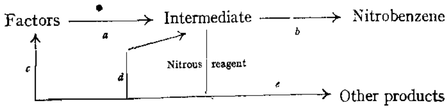
(Sections 9 and 10) DISCUSSION.

## (9) *Mechanism of Nitration in Nitromethane Solution.*

(a) *Nitration of Benzene.*—The principal facts to be explained are as follows (Section 5). With nitric acid in large and substantially constant concentration, the reaction is of order zero. Nitrous acid, or, more accurately, some substance which in the water-diluted solution is estimated as nitrous acid, decelerates reaction according to the law, $k_0 = 1/(a + b\sqrt{n})$, where $k_0$ is the measured rate constant and $n$ the equivalent nitrous acid concentration. Nitrous acid does this without appreciably changing its own concentration in the course of reaction, and without disturbing the zero-order law. The reaction is strongly accelerated by increasing the nitric acid concentration, but this involves no disturbance either to the zero-order time law, or to the form of the nitrous acid rate law; indeed, the acceleration is the joint result of comparable decreases of the nitrous-acid-dependent and nitrous-acid-independent parts of the reciprocal rate. The reaction is accelerated by rise of the temperature, and this acceleration also arises from comparable changes in the two parts of the reciprocal rate.

The zero-order time law shows at once that the slowest stage of the complete process does not involve benzene: we have to decide what it does involve. Nitrous acid, and products dependent on it, are excluded by the observation that the time law remains the same at the lowest attainable concentrations of nitrous acid. Responsibility for the time law thus lies between nitric acid and nitromethane. It is unlikely that nitric acid is the sole reagent for the slow process, first, because it is difficult to think of a probable change, and secondly, because in nitrations by means of nitric acid with sulphuric acid as solvent the reaction order with respect to the aromatic compound is not zero but one (Section 1, c): this seems to make the nitromethane at least partly responsible for the time law. The possibilities are that nitromethane is the sole reagent, with nitric acid as a possible catalyst, and that nitromethane and nitric acid interact as direct reagents; we might, for instance, assume $CH_3{\cdot}NO_2 \longrightarrow CH_2{:}NO{\cdot}OH$, or $CH_3{\cdot}NO_2 + HNO_3 \longrightarrow NO_2{\cdot}CH_2{\cdot}NO_2 + H_2O$, or some other kinetically equivalent isomerisation or condensation. Because we cannot explain the part played by nitrous acid without postulating *two* low-concentration intermediates in the nitration, we shall actually use a combination of these ideas.

The reason why one low-concentration intermediate will not explain the facts can be understood without entering into the quantitative details of the nitrous acid effect. Suppose we set up a one-intermediate scheme, *viz.*, the reactions *a* and *b* represented below, *a* being the slow process, involving nitromethane and possibly nitric acid, and *b* the rapid process. We then have to explain the decelerating action of nitrous acid by supposing that it, or something derived from it—we may call this shortly the "nitrous reagent"—reacts with the intermediate. The reaction or chain of reactions thus set up might terminate (*c*) with the factors, (*d*) with the single postulated intermediate, or (*e*) with other substances:




We shall find that there are objections to all these alternatives, though *c* and *d* are at first sight attractive, since they complete cyclic processes whereby the nitrous reagent could be regenerated, thus affording an explanation for the fact that the amount of it which disappears is inappreciable. We exclude alternative *c*, since it would amount to a catalytic shifting of the pseudo-equilibrium between factors and intermediate, and the shift would be in the direction of the factors. It is true that a catalyst may shift an equilibrium if there is sufficient of it; but in our case the direction of the shift is wrong, because, although the concentration of the nitrous reagent may be much larger than that of the intermediate, it must be very small compared with those of the factors. Therefore the nitrous reagent

cannot alter the free energy of the latter, and its assumed effect must be envisaged as an increase of the partial molar free energy and fugacity of the intermediate. This implies repulsive forces between the intermediate and the nitrous reagent, and, further, that these entities would, in dilute solution, stay in each other's force-range in the presence of such forces—an absurd conclusion. Alternative *d* can at once be dismissed because, in the steady state, just as many molecules of the intermediate would be regenerated per second as were being destroyed by the nitrous reagent; thus the stationary concentration of intermediate, and the rate of production of nitrobenzene from it, would be unaffected, and the known influence of the nitrous reagent would remain unexplained. Reactions *e* would normally destroy potential nitrous acid, and, since we know that the amount destroyed is small compared with the initial amounts of nitrous acid and of benzene, we have to assume that the consumption of intermediate by route *e* is small relatively to its consumption by route *b*. But that is exactly what we must not assume if reactions *e* are to explain the decelerating effect. The possibility that potential nitrous acid is regenerated by some chain mechanism in reactions *e* is also excluded, because in any case, if we are to explain the anticatalysis, route *e* must absorb intermediate, and therefore, indirectly, factors, in quantity comparable to the quantity of nitrobenzene formed. But we know, from experiments with smaller concentrations of nitric acid than were taken for the kinetic measurements, that the alkalimetrically-measured amounts of nitric acid consumed agree with the titanometrically-determined quantities of nitrobenzene formed, leaving no margin for an appreciable consumption of nitric acid by any route other than nitration.

Because all one-intermediate schemes break down, we postulate two low-concentration intermediates. They are obtained by combining the possibilities already mentioned, *viz.*, the isomerisation of nitromethane and its condensation with nitric acid. We can then associate a nitrous acid reaction of type *e* with an intermediate which does ***not*** directly produce nitrobenzene: this is essential for the avoiding of the difficulties mentioned. The isomerisation would evidently be the first reaction, and the nitric acid condensation the second, since only the latter could give an active nitrating agent. Further, the isomerisation will certainly be strongly reversible, and the subsequent condensation with nitric acid is sure to be slightly reversed in the presence of the water it produces. Thus the preliminary system consists in reactions (1)—(4), supplemented by a nitrous acid reaction (5), which has to be further considered. In reaction (6) the second intermediate nitrates the benzene, being thereby reconverted into the first:

$$CH_3{\cdot}NO_2 \underset{(2)}{\overset{(1)}{\rightleftharpoons}} CH_2{:}NO{\cdot}OH \underset{(4)\ H_2O}{\overset{(3)\ HNO_3}{\rightleftharpoons}} CH_2{:}NO{\cdot}O{\cdot}NO_2 \qquad \text{(Scheme I)}$$

$$CH_2{:}NO{\cdot}OH \xrightarrow{(5)\ HNO_2} \text{“Nitrous products”} \qquad CH_2{:}NO{\cdot}O{\cdot}NO_2 \xrightarrow{(6)\ C_6H_6} CH_2{:}NO{\cdot}OH$$

This cyclic linking of the two intermediates, which follows automatically from the rest of the scheme, is also essential to the interpretation of the qualitative observations: unless there were some such regenerative process, we could not explain why an inconsiderable consumption of nitrous acid produces a large effect on the reaction speed. Thus scheme I seems to provide the simplest possible basis for an attempted interpretation. On account of the chosen experimental conditions, we disregard the reactions (reversible proton-transfer) between nitric acid and water; these reactions would, however, play an essential part in the treatment of the more general kinetic problem which arises on removing the restriction that the proportion of nitric acid is large:

$$HNO_3 + H_2O \underset{(8)}{\overset{(7)}{\rightleftharpoons}} NO_3^- + H_3O^+ \qquad \text{(I; 7, 8)}$$

It is convenient to divide the quantitative treatment of the nitrous acid effect into two parts. We first consider why the significant power of the nitrous acid concentration is the square root. This point is dealt with simply by choosing the right form for reaction (5) in scheme I. It is assumed that what is estimated as nitrous acid is present in the nitration solutions almost wholly as a molecule which decomposes rapidly, slightly, and reversibly into two molecules, one of which is the "nitrous reagent." Reasonable details are easily

supplied: in the strongly dehydrating conditions of the nitration mixtures, nitrous acid is likely to exist almost wholly as dinitrogen trioxide, and this is known to be dissociated rapidly, slightly, and reversibly into nitric oxide and nitrogen dioxide. The rate of any reaction involving a single molecule of either of the last-named oxides would be some function of the square root of the equivalent nitrous acid concentration:

$$2HNO_2 \rightleftharpoons N_2O_3 + H_2O \qquad N_2O_3 \rightleftharpoons NO + NO_2 \qquad (I;\ 5)$$
$$[\text{stoicheiometric } HNO_2] \approx [N_2O_3] = K[NO][NO_2] = K[NO]^2 = K[NO_2]^2$$

As to the mode of action of the "nitrous reagent" we can only surmise. One possibility, mentioned solely as an illustration, is that nitrogen dioxide adds slowly to the unsaturated link in *aci*nitromethane, forming a free radical, which in the oxidising surroundings rapidly loses a hydrogen atom to give dinitromethane.

$$NO_2 + CH_2{:}NO_2H \xrightarrow[\text{(slow)}]{} NO_2{\cdot}CH_2{\cdot}NO_2H \xrightarrow[\text{(fast)}]{} CH_2(NO_2)_2 + H \qquad (I;\ 5)$$

The second part of the problem is to explain why the function expressing the dependence of the rate on the square root of the nitrous acid concentration is the reciprocal of a linear function of the latter, *viz.*, $k_0 = 1/(a + bn^{\frac{1}{2}})$. The interpretation of this cannot now be assisted by *ad hoc* choice of the details of reaction, and our only course is to ascertain whether the scheme already developed from other considerations leads to the required relationship.

We consider the steady state of reaction in which the two intermediates have small, and therefore in an absolute sense only slowly varying, concentrations. Let $v_1, v_2, \ldots v_6$ be the *instantaneous* rates of the reactions (1), (2), . . . (6) of scheme I, $v$ being the measured rate of nitration. The rate of formation of the first intermediate from nitromethane is $v_1$. The fraction of first intermediate which passes into the second intermediate is $f_I = v_3/(v_2 + v_3 + v_5)$, so that the rate of formation of the second intermediate in this direct way is $v_1 f_I$. This follows because the amount of material stored in the form of first intermediate is effectively zero and therefore effectively constant. The fraction of the second intermediate that enters into nitration is $f_{II} = v_6/(v_4 + v_6)$, so that the rate of nitration by the route specified is $v_1 f_I f_{II}$. This is true because the storage of material as second intermediate is effectively zero and hence effectively invariant. The rate of regeneration of the first intermediate from second intermediate, formed as described, is $v_1 f_I$, and hence the extra rate of production of second intermediate from material that has gone once round the reaction cycle is $v_1 f_I^2$. The consequential extra rate of nitration will be $v_1 f_I^2 f_{II}$. Continuing this argument we find:

$$v = v_1(f_I + f_I^2 + f_I^3 + \ldots)f_{II} = v_1 f_I f_{II}/(1 - f_I) = v_1 v_3 v_6/(v_2 + v_5)(v_4 + v_6)$$

We know that $v$ is independent of the time. Since $v_4$ will always involve the time owing to the progressive accumulation of water during nitration, the expression on the right cannot be independent of the time unless $v_6 \gg v_4$, in which case it reduces to $v_1 v_3/(v_2 + v_5)$. In order to see if this obviously necessary condition for time-invariance is also sufficient, we replace these instantanious rates by rate constants and appropriate functions of the reagent concentrations: $v_1 = k_1\phi_1(M)F_1(N)$, $v_2 = k_2M^*F_2(N)$, $v_3 = k_3M^*F_3(N)$, $v_5 = k_5M^*n^{\frac{1}{2}}F_5(N)$. Here $M$ is the concentration of nitromethane, $M^*$ that of *aci*nitromethane (first intermediate), and $N$ and $n$ those of nitric and nitrous acids. Since the concentrations of nitromethane and nitric acid are large, they occur in the equations in the form of functions $\phi_1$, $F_1$, $F_2$, $F_3$, $F_5$ which cannot be specified: we cannot even assert that $F_1$ and $F_2$ are the same, as they would be for thermodynamic reasons if $N$ were considerably smaller than it is. However, the only concentration which can exhibit a considerable *proportional* variation with time is $M^*$, and this disappears from the final equation by cancellation; thus $v$ becomes independent of the time and may be replaced by $k_0$:

$$k_0 = \frac{k_1\phi_1(M)F_1(M) \,.\, k_3F_3(N)}{k_2F_2(N) + k_5n^{\frac{1}{2}}F_5(N)} \quad \ldots \ldots \quad (6)$$

This equation (6) is obviously identical with the empirical equation (1), and thus our reaction

scheme gives a satisfactory account of the observed rate laws. The values of $a$ and $b$ are interpreted thus:

$$a = \frac{k_2}{k_1 k_3} \cdot \frac{F_2(N)}{\phi_1(M) \cdot F_1(N) \cdot F_3(N)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$b = \frac{k_5}{k_1 k_3} \cdot \frac{F_5(N)}{\phi_1(M) \cdot F_1(N) \cdot F_3(N)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

These equations, (7) and (8), have to be compared with equations (2) and (3). Since the proportional variation of $M$ is small in the experiments, $\phi_1(M)$ will be a linear function of $M$, that is, of $27 - N$. Taking $\phi_1$ as proportional to $27 - N$, the theoretical and empirical equations agree if $F_1F_3/F_2 = N^6$ and $F_1F_3/F_5 = N^5$ within the range of variation of $N$. On general grounds we expect $F_3$ to be particularly sensitive to $N$, and to account to a considerable extent for these high indices.

The temperature-variable parameters $A$ and $B$ are given (except possibly for a constant) by the equations

$$A = k_2/k_1k_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

$$B = k_5/k_1k_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

Equations (9) and (10) are consistent in form with the empirical equations (4) and (5). This follows because $k_1, k_2, k_3$, and $k_5$ are expected separately to obey the Arrhenius equation; so that $A$ and $B$ will satisfy equations of the same form, and their logarithms will be linear functions of temperature for the short temperature ranges considered. If $E_1$, $E_2$, $E_3$, and $E_5$ are the energies of activation of the four reactions, our results for the temperature-variation of $A$ and $B$ receive the interpretation:

$$E_1 + E_3 - E_2 = 15; \qquad E_1 + E_3 - E_5 = 19 \text{ kilocals.}$$

Since most reactions that go with observable velocities near room temperature have energies of activation of the order of 20 kilocals., it seems consistent that values of this order are interpreted as combinations of three such energies, two with positive signs and one with a negative sign.

(b) *Nitration of Toluene and Ethylbenzene.*—The facts to be explained (Section 6) are that the nitrations of these substances are reactions of order zero, with absolute rates always equal to each other and to the rate for the nitration of benzene under the same conditions with regard to temperature and the concentrations of nitric and nitrous acids.

It is known that electron-releasing alkyl groups enhance the reactivity of the benzene ring towards electrophilic reagents. Nitration is an electrophilic substitution, and in Part II (J., 1931, 1959) it was shown that toluene is nitrated about 25 times faster than benzene when the same nitrating agent competes for the two hydrocarbons. Presumably ethylbenzene would be found to nitrate a little faster than toluene in experiments of this type. Now, in experiments by the competitive method, the reactions whose rates are compared are those in which the aromatic compounds are directly concerned; *i.e.*, they are of the type of reaction 6 of scheme I. Therefore, whilst reactions 1—5 of scheme I remain the same, independently of what is being nitrated, reaction 6 will depend on the aromatic compound and will have greater specific rates for toluene and ethylbenzene than for benzene. But we have seen that, so long as $v_6$ is sufficiently larger than $v_4$ to enable the latter to be neglected in comparison, *both* $v_4$ *and* $v_6$ disappear from the rate equation, thus eliminating the dependence of the measured rate both on the substance which is being nitrated and on the time: the rate is determined solely by reactions (1), (2), (3), and (5). It is evident that, if the necessary condition relating to $v_6$ and $v_4$ is fulfilled for benzene, it will be, with a still larger margin, for toluene and ethylbenzene. Hence the measured rate for these substances, as for benzene, will be independent of the time, and also independent of the substance.*

* One sees at once from this example why the competitive method, and not the kinetic method, is the right one for measuring the relative rates of nitration of aromatic compounds (cf. Part III, this vol., p. 907).

(c) *Nitration of the Halogenobenzenes.*—The facts to be explained are as follows (Section 7). For all four halogenobenzenes the measured rates of nitration are smaller than for benzene in two degrees, a lesser degree for fluoro- and iodo-benzene and a greater degree for chloro- and bromo-benzene (H>F,I>Cl,Br). For all four halogenobenzenes the effective reaction order is greater than zero, although for none is it greater than unity; and it is greater than zero in two degrees, a lesser degree for fluoro- and iodo-benzene and a greater degree for chloro- and bromo-benzene (0 = H<F,I<Cl,Br). The effective reaction order is not independent of time, but invariably rises during a run; in the case of chloro- and bromo-benzene it closely approaches unity towards the end of a run. As in the case of benzene, nitrous acid decreases the rate, whilst an increased concentration of nitric acid strongly increases the rate.

It is known that the electron-attracting halogen atoms decrease the reactivity of the benzene ring towards electrophilic reagents. In Part IV (preceding paper) it was shown that fluoro- and iodo-benzene are nitrated about 6 times, and chloro- and bromo-benzene about 30 times, slower than benzene when the same nitrating agent competes for halogenobenzenes and for benzene. Since these experiments measure the relative rates of reactions of the type of reaction (6) in scheme I, we have an obvious explanation for the facts noted above: in the nitration of the halogenobenzenes $v_6$ is no longer sufficiently greater than $v_4$ to enable the latter to be neglected. Intuitively one can see that under these conditions the relative reactivities of the halogenobenzenes, that is, their rates in reaction 6, will to some extent be reflected in the measured rates, and that, depending on the degree to which this is so, the effective reaction orders will be greater than zero.

To control intuition, and obtain further details concerning the consequences of the theory, we must examine the generalised rate equation:

$$v = v_1v_3v_6/(v_2 + v_5)(v_4 + v_6)$$
$$= \frac{k_1\phi_1(M)\mathrm{F}_1(N) \, . \, k_3\mathrm{F}_3(N) \, . \, k_6[\mathrm{Arom.}]\mathrm{F}_6(N)}{\{k_2\mathrm{F}_2(N) + k_5n^t\mathrm{F}_5(N)\}\{k_4[\mathrm{H_2O}]\mathrm{F}_4(N) + k_6[\mathrm{Arom.}]\mathrm{F}_6(N)\}} \quad . \quad . \quad (11)$$

Here Arom. stands for the aromatic compound and $\mathrm{F}_4$ and $\mathrm{F}_6$ are new unknown functions of the nitric acid concentration. (The concentration $M^{**}$ of the second intermediate, like $M^*$, the concentration of the first, disappears by cancellation.) There are three special cases.

The first is the limiting case already considered (and realised), in which $v_6 \gg v_4$ over practically the whole experimental range: $v$ is then independent of time, of [Arom.], and of $k_6$.

The second is an intermediate critical case in which, not merely are $v_6$ and $v_4$ comparable, but, more particularly, $k_4\mathrm{F}_4(N)$ equals $k_6\mathrm{F}_6(N)$ precisely. Since for stoicheiometric reasons [Arom.] + [$\mathrm{H_2O}$] is constant, the second factor of the denominator of equation (11) will now be constant, and therefore $v$ will be proportional to [Arom.]; that is, the reaction will be accurately of the first order throughout its course.

The third is the opposite limiting case in which $v_6 \ll v_4$ over practically the whole experimental range: this means that $v$ will be proportional to [Arom.]/[$\mathrm{H_2O}$], *i.e.*, to [Arom.]/{[Arom.]$_0$ — [Arom.]}, so that the reaction will start relatively extremely rapidly and end relatively very slowly.

Throughout the whole region between the first limiting case and the critical case, the effective reaction order will be between zero and unity; and it will rise during a run, approaching unity asymptotically towards the end of reaction. This can be seen as follows. In the case considered, $k_6\mathrm{F}_6(N)$ is greater, but not enormously greater, than $k_4\mathrm{F}_4(N)$. Expressing these factors as $N_6$ and $N_4$, writing $x$ for [Arom.], and omitting factors which are independent of the time, we find:

$$v \propto \frac{N_6x}{N_4(x_0 - x) + N_6x} \propto \frac{N_6}{N_4} \cdot \frac{x}{x_0} \cdot \left[1 + \frac{N_6 - N_4}{N_4} \cdot \frac{x}{x_0}\right]^{-1}$$

This means that, so long as $x/x_0$ is not small, *i.e.*, near the commencement of reaction, $v$ will diminish with time more slowly than $x$ does, so that the *initial* effective reaction order

will have some definite value between zero and unity; when, however, $x/x_0$ becomes small, near the end of reaction, $v$ will become asymptotically proportional to $x$, and the effective reaction order will rise asymptotically to unity.

Throughout the whole region between the critical case and the second limiting case, the effective reaction order will be between unity and infinity; and it will fall during a run, approaching unity asymptotically towards the end of reaction. The law of variation of $v$ with time will be that just formulated, with $(N_6 - N_4)/N_4$ now a negative quantity: $v$ will decrease with time more rapidly than $x$ does as long as $x/x_0$ is not small; but when it becomes small, then $v$ will be proportional to $x$.

Now we know that benzene belongs to the first limiting case ($v_6 \gg v_4$). It does this so definitely and accurately (as shown by the absence of curvature near the end of the reaction–time curves) that a reduction in the specific rate of reaction (6) by factors of the order of only 6, or even 30, cannot be expected to displace the example from the first limiting case across the critical case into the region between the latter and the second limiting case. It is therefore satisfactory that in order to account for our results we have to assume that the halogenobenzenes fall in the region between the first limiting case and the critical case: $k_6F_6(N)$ is greater than $k_4F_4(N)$, but not incomparably greater. With this assumption the detailed interpretation follows immediately. In the nitration of fluoro- and iodo-benzene, for which the differences between $k_6F_6(N)$ and $k_4F_4(N)$ are still relatively large, the measured reactions are slower than for benzene, and their effective orders, not much above zero near the commencement of nitration, rise in the direction of unity towards the end. In the nitration of chloro- and bromo-benzene, for which $k_6F_6(N)$ is not much larger than $k_4F_4(N)$, the measured reactions are still slower, and their effective orders, which are considerably above zero at the commencement of nitration, become asymptotically equal to unity near the end.

From the form of equation (11) it is easily seen that nitrous acid must decelerate the measured reaction qualitatively as for the special case governed by equation (6). Except in the unlikely event of $F_6/F_4$ varying as a large negative power of $N$, the measured rate will increase rapidly with the nitric acid concentration in the general case of equation (11), as it has been shown to do in the special case of equation (6). Thus all the qualitative observations are explained.

(d) *Expression of the Mechanism as a Chain Reaction.*—The nature of the process elucidated in the foregoing section is best appreciated by writing it as a chain-reaction. The fundamental chain-mechanism is as follows:

*Chain initiation*:

$$CH_3{\cdot}NO_2 \longrightarrow CH_2{:}NO{\cdot}OH \text{ (catalysed by } HNO_3)$$

*Chain propagation*:

$$\begin{cases} CH_2{:}NO{\cdot}OH + HNO_3 \longrightarrow CH_2{:}NO{\cdot}ONO_2 + H_2O \\ CH_2{:}NO{\cdot}ONO_2 + HAr \longrightarrow CH_2{:}NO{\cdot}OH + NO_2{\cdot}Ar \end{cases}$$

*Chain destruction (normal)*:

$$CH_2{:}NO{\cdot}OH \longrightarrow CH_3{\cdot}NO_2 \text{ (catalysed by } HNO_3)$$

In addition there is a reaction which renders ineffective individual " links " in the " chain " without breaking the chain as a whole; and also a further method of chain destruction:

*Link destruction*:

$$CH_2{:}NO{\cdot}ONO_2 + H_2O \longrightarrow CH_2{:}NO{\cdot}OH + HNO_3$$

*Chain destruction (abnormal)*:

$$\begin{cases} 2HNO_3 \rightleftharpoons N_2O_3 + H_2O \rightleftharpoons NO + NO_2 + H_2O \\ CH_2{:}NO{\cdot}OH + NO_2 \longrightarrow CH_2(NO_2)_2 + H \end{cases}$$

(or some other reaction between $CH_2{:}NO{\cdot}OH$ and NO or $NO_2$).

(10) *Nitrating Agents and the Rôle of Solvents in Nitration.*

The unexpected conclusion that nitromethane functions as a convenient nitration solvent simply because its *aci*-form can give rise to a mixed anhydride with nitric acid, suggests a correlation between this and several other conclusions and observations. We have, for example, classified nitration solvents into three groups (Section 4): in most neutral organic solvents, *e.g.*, dioxan or acetonitrile, nitration is very slow; in acetic anhydride and nitromethane it proceeds at a medium rate; in sulphuric acid it is very fast. In sulphuric acid the reaction is bimolecular, the rate being proportional to the stoicheiometric concentration of nitric acid; and the same is true when the nitrating agent is introduced as dinitrogen pentoxide, the kinetic effect of which is the same as that of twice as many molecules of nitric acid (Section 1, c). The fact that the solvents acetonitrile and nitromethane, which for most reactions behave very similarly, are strongly differentiated with respect to nitration is significant in connexion with the conclusion that the *aci*-form of nitromethane plays an essential rôle.

We are familiar with the idea that the efficacy of brominating agents X·Br depends on the affinity of X for the electrons of the X·Br bond, since this determines the affinity of the bromine atom for the aromatic electrons: Cl·Br is a better brominating agent than Br·Br, which is in turn better than OH·Br (Ingold, Smith, and Vass, J., 1927, 1245). It may now be suggested that nitrating agents are always of the form $X{\cdot}NO_2$, their efficacy being determined by the electron-affinity of X, as indicated, for instance, by the acid-strength of X·H. If this is true, the nitric acid molecule itself, $HO{\cdot}NO_2$, *i.e.*, nitric acid in not too concentrated solutions in inert solvents, would be a weak nitrating agent, corresponding to the very weakly acidic character of water, HO·H. In nitromethane and acetic anhydride solutions, the nitric acid becomes acylated, and the product $AcO{\cdot}NO_2$ is a more active nitrating agent, in agreement with the greater acidity of the organic acids AcO·H. In sulphuric acid solution, $SO_4H{\cdot}NO_2$ can be formed (as it surely will be when dinitrogen pentoxide is employed) and this would be a powerful nitrating agent for the reason which makes $SO_4H{\cdot}H$ a very strong acid.

The hydroxonium ion, $H_3O^+$, is to be regarded as an acid, which is not so strong as sulphuric acid, but yet much stronger than acids obeying the dilution law. Therefore $H_2O^+{\cdot}NO_2$ should be a very active nitrating agent. Hantzsch has shown (*Ber.*, 1925, **58**, 941) that in nearly absolute nitric acid protons are transferred from one molecule of nitric acid to another with the production of $NO(OH)_2{}^+$ and $N(OH)_3{}^{++}$, the perchlorates of which he and Wolf isolated. He surmised that the second of these might be the nitrating agent of "mixed acid," whilst Brewin and Turner (J., 1928, 334) suggested $N(OH)_4{}^+$. Our point of view leads us to suppose that the first of Hantzsch's cations, in its tautomeric form $NO_2{\cdot}OH_2$, is the nitrating agent of fuming nitric acid: the other cations have not the right type of structure. In "mixed acid" $NO_2{\cdot}OH_2{}^+$ and $NO_2{\cdot}SO_4H$ may both occur, and both should be highly active.

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## 178. *The Thermal Decomposition of Ammonium Dichromate.*

By E. H. Harbard and A. King.

On ignition of ammonium dichromate in a vacuum or at atmospheric pressure, at a temperature below its normal point of decomposition, a black product is obtained which has been variously identified as hydrated chromic oxide or chromium dioxide, but as it has now been shown that nitrogen and nitrous oxide are evolved in its decomposition, it is probably a solid solution of two or more compounds.

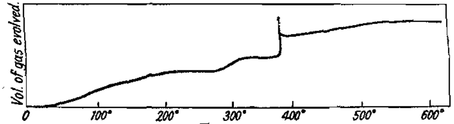
On ignition of the above material or on the direct thermal eruption of ammonium dichromate, an olive-green voluminous powder is obtained which is usually assumed to be chromic oxide. As a result of numerous analyses it is now established that this compound contains more oxygen than does chromic oxide, and that the excess

oxygen is not easily lost on reduction with hydrogen. This compound is probably a non-stoicheiometric oxide of chromium.

ALTHOUGH the decomposition of ammonium dichromate is still usually represented as $(NH_4)_2Cr_2O_7 \longrightarrow Cr_2O_3 + N_2 + 4H_2O$, previous workers have noticed that ammonia and oxides of nitrogen are present in appreciable quantities amongst the products.

By heating ammonium dichromate for a considerable time just below the temperature at which it normally decomposes violently, Ball (J., 1909, **95**, 87) obtained a homogeneous black powder which he identified as hydrated chromium dioxide, $3CrO_2,H_2O$; considerable quantities of ammonia and oxides of nitrogen were evolved in this reaction. Hooton (*Proc. Roy. Soc.*, 1908, **24**, 27) obtained a black product under similar conditions but formulated it as $H_2Cr_2O_4$; heated in oxygen, it formed $2CrO_2,H_2O$. Moles and Gonzalez (*Anal. Fis. Quim.*, 1923, **21**, 204), using a similar method of preparation, obtained a black crystalline compound which they identified as $CrO_2$ by ignition to chromic oxide. Fischbeck and Spingler (*Z. anorg. Chem.*, 1938, **235**, 185) have now described the preparation of a black compound by decomposing ammonium dichromate at a pressure of about $10^{-4}$ mm. and indicate that it has the composition $Cr_2O_3,H_2O$, the decomposition being represented as $(NH_4)_2Cr_2O_7 = N_2 + Cr_2O_3,H_2O + 3H_2O$. Apparently, most of these earlier workers analysed their compounds by ignition to an end product presumed to be chromic oxide; but (see p. 957) this assumption is hardly permissible.

As a prelude to the study of the surface properties of the oxides of chromium, we carried out the decomposition of ammonium dichromate in a vacuum and obtained a light, black, hygroscopic powder which appeared under the microscope to be highly porous but homogeneous; it was insoluble in all acids and in aqueous solutions of alkalis. In view of the disagreement as to the composition of this material we investigated it. The washed and dried powder was quantitatively analysed for chromium by alkaline fusion and conversion into dichromate. A weighed quantity of the material was then decomposed by heating it in a closed tube, the gas evolved being collected in a gas burette. The system was allowed to reach equilibrium before each increase of temperature. The decomposition curve, plotted in the figure, is rather indeterminate but it certainly does




not represent the mere dissociation of a hydrate or higher oxide. The peculiar shape of the curve in the neighbourhood of 385° was due to a sudden decomposition, followed by rapid absorption of part of the gaseous products. A portion of the gas was analysed and proved to be a mixture of equal volumes of nitrogen and nitrous oxide. As water also appeared to be produced by the decomposition, a determination of water was carried out on a further sample. The full analysis was Cr, 61·2; $N_2$, 3; $N_2O$, 4·5; $H_2O$, 2; $O_2$ (by diff.), 29·3%. In spite of its apparent homogeneity, it thus seems extremely doubtful if this powder is a true compound, and it certainly does not possess any of the simple formulæ given to it by the previous workers. It is probably a solid solution of two or more compounds or else a surface compound.

A further point of interest concerns the solid product of decomposition of ammonium dichromate at higher temperatures, usually assumed to be chromic oxide. Other workers have commented on the heterogeneous appearance of this material, which usually consists of dark olive-green flakes mixed with a smaller amount of a black substance. On heating the black powder discussed above, an olive-coloured product was obtained. This was analysed for chromium; the results tabulated below show (No. 1) that the percentage of chromium is below that corresponding to chromic oxide. Prolonged ignition only increased this percentage slightly.

| No. | Oxide. | Cr, %. |
|---|---|---|
| 1 | Residue of ignition of black powder at 350° | 67·3 ± 0·5 |
| 2 | Olive-green and black oxide obtained by heating ammonium dichromate in air in the Bunsen flame | 67·5 ± 0·4 |
| 3 | No. 2 heated strongly over Meker burner | 67·8 |
| 4 | No. 2 reduced in hydrogen for 2 hrs. at 750° | 67·6 |
| 5 | No. 2 ,, ,, ,, 4 hrs. at 750° | 68·1 |
| 6 | No. 2 ,, ,, ,, 21 hrs. at 800° | 68·4 |
| 7 | Chromic oxide formed by heating mercurous chromate | 68·4 |

An analysis was then made of the olive-green and black residue formed by the direct decomposition of ammonium dichromate at atmospheric pressure. The results (No. 2) show that this also is not pure chromic oxide. At first it was thought that this residue was a mixture of two compounds, the olive chromic oxide together with small quantities of a black higher oxide. A quantity of the black flakes was therefore separated mechanically from the main bulk. These were extraordinarily porous but underwent no decomposition below 800° although the colour changed to olive-green in the process. The black compound was thus probably another modification of chromic oxide.

Reduction of the olive-green oxide took place only slowly in hydrogen, but after 21 hours at 800° there was complete transformation into chromic oxide. It was noticed that, after reduction, the voluminous olive-green powder had changed into a compact bright green powder similar in appearance to chromic oxide prepared by ignition of chromic anhydride or mercurous chromate.

From these data it may be concluded that the olive-green oxide resulting from the decomposition of ammonium dichromate is an oxide of chromium containing rather more oxygen than is required by the formula $Cr_2O_3$. This excess of oxygen may be present as a surface oxide, but the difficulty of reduction and other considerations tend to indicate that it is a non-stoicheiometric compound.

## Experimental.

*Decomposition of Ammonium Dichromate in a Vacuum.*—A quantity of powdered ammonium dichromate of tested purity was placed in a small bulb from which a length of wide glass tubing led to a trap filled with tightly packed glass-wool. The system was evacuated by means of an oil-pump, and the dichromate heated. Explosive decomposition of the salt took place, and the solid product, a voluminous black powder, was ejected into the trap, the pump being kept running during the reaction. The product was well washed with water to free it from undecomposed ammonium dichromate, a precaution apparently neglected by most of the earlier workers, and dried by heating at 150°. Analysis of this compound was rather difficult since it tended to decompose slightly while still moist. The chromium analysis quoted (No. 1) is the mean of six determinations.

*Analysis of the Olive-green Oxide.*—The results quoted in the table were obtained by volumetric analysis of the dichromate formed by fusion of the oxide with sodium peroxide. The result (No. 2) is the mean of 8 determinations and was also checked by gravimetric analysis in which a known weight of the pure ammonium dichromate was ignited and the residue weighed.

Imperial College, London, S.W. 7.

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# 179. *Experiments with Heavy Water on the Acid Hydrolysis of Esters and the Alkaline Decomposition of Diacetone Alcohol.*

By W. E. Nelson and J. A. V. Butler.

Experiments have been made on the rates of hydrolysis of ethyl formate and methyl acetate in hydrochloric acid solutions in mixtures of water and deuterium oxide. The observations are in reasonable agreement with the calculated " thermodynamic " curves indicating that the reaction proceeds by way of an intermediate complex, probably $\overset{H^+}{R\cdot CO\cdot OR'}$, which is in thermodynamic equilibrium with the medium. This reaction should not therefore be subject to general acid catalysis.

Similar experiments were made with the alkaline decomposition of diacetone alcohol,

and the " thermodynamic " curve of an alkaline reaction has been calculated for comparison. The actual curve of the reaction rate against the deuterium content of the solution is more exactly linear than the calculated curve, but the difference is too small to be conclusive. The substitution of hydrogen by deuterium in the diacetone alcohol decreases the reaction rate, indicating that the rate-determining step is the transfer of a proton from the alcohol to $OH^-$ (or $OD^-$):

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}C(OH)(CH_3)_2 + OH^- \longrightarrow CH_3{\cdot}CO{\cdot}CH_2{\cdot}C\begin{cases}CH_3\\(OH)\\CH_2^-\end{cases} + H_2O$$

$$\downarrow$$

$$[CH_3{\cdot}CO{\cdot}CH_2]^- + CH_3{\cdot}C(OH){:}CH_2,$$

giving an ion which can immediately split into a molecule and ion of enolic acetone. This mechanism explains all the main features of the reaction.

THE use of deuterium compounds has provided a means of distinguishing in suitable cases the various mechanisms of acid- or base-catalysed reactions. It has been found that in some cases the reaction rate is increased and in others decreased by the substitution of deuterium oxide for water in the solvent. It was first suggested (Wynne-Jones, *Chem. Reviews*, 1935, **17**, 115) that, in reactions which are faster in light than in heavy water, the rate-determining step is a proton transfer, while in the reverse case there is an equilibrium between the substrate and hydrogen ions of the type $S + H_3O^+ \rightleftharpoons SH^+ + H_2O$, the concentration of the complex $SD^+$ being greater than that of $SH^+$ (Bonhoeffer and Moelwyn-Hughes, *Z. physikal. Chem.*, 1934, *B*, **26**, 272). In the latter case the complex should be in thermodynamic equilibrium with the medium, and the rate should be determined by the respective proton and deuteron activities of the solution. The former case thus corresponds to Brönsted's definition of general acid catalysis, and the latter to specific hydrogen-ion catalysis. The criterion is not, however, conclusive. Reitz has shown (*Z. physikal. Chem.*, 1937, *A*, **179**, 119) that in the bromination of light acetone, which was apparently a well-established case of general catalysis, the reaction is quicker in heavy than in light water and the variation of the rate with the deuterium content follows the equilibrium curve. The enolisation of acetone involves both acidic and basic catalysis, *viz.*,

$$CH_3{\cdot}CO{\cdot}CH_3 \underset{A^-}{\overset{AH}{\rightleftharpoons}} CH_3{\cdot}C(OH^+){\cdot}CH_3 \xrightarrow{B} CH_3{\cdot}C(OH){:}CH_2$$

and these observations indicate that equilibrium is established in the first stage but not in the second. This is confirmed by the fact that " heavy " acetone reacts more slowly than light in all media. It is clear that conclusions drawn from the relative rates in light and in heavy water should be controlled whenever possible by the use of reactants containing deuterium.

The thermodynamic proton and deuteron activities in an aqueous solution may be expressed as

$$\alpha_{H^+} = \frac{\Sigma H_3O^+ . f^+[H_2O]^{\frac{1}{2}}}{Q'(n)}; \quad \alpha_{D^+} = \frac{\Sigma H_3O^+ . f^+[D_2O]^{\frac{1}{2}}}{Q'(n)\sqrt{L}}$$

where $Q'(n)$ is a function, the nature of which has been established empirically by equilibrium measurements (Gross, Steiner, and Süss, *Trans. Faraday Soc.*, 1936, **32**, 883; Orr and Butler, J., 1937, 330). An assumption which permits its theoretical calculation has been suggested recently by Schwarzenbach (*Z. Elektrochem.*, 1938, **44**, 48). With the following equilibrium constants: *

$$k_1^{+H} = [H_3O^+]/[H_2O]\alpha_{H^+} \qquad 3k_1^{+D} = [H_2DO^+]/[H_2O]\alpha_{D^+}$$
$$\tfrac{3}{2}k_2^{+H} = [H_2DO^+]/[HOD]\alpha_{H^+} \qquad \tfrac{3}{2}k_2^{+D} = [HD_2O^+]/[HOD]\alpha_{D^+}$$
$$3k_3^{+H} = [HD_2O^+]/[D_2O]\alpha_{H^+} \qquad k_3^{+D} = [D_3O^+]/[D_2O]\alpha_{D^+}$$

* The statistical factors 3 and $\frac{3}{2}$ are introduced here explicitly, whereas in Orr and Butler's paper they were contained in the constant; *i.e.*, $\frac{3}{2}k_2^{+H}$ is identical with Orr and Butler's $k_2^{+H}$.

Schwarzenbach's assumption is equivalent to

$$k_1^{+H}/k_1^{+D} = k_2^{+H}/k_2^{+D} = k_3^{+H}/k_3^{+D}$$

by which the equations connecting these constants can be solved, giving

$$\frac{k_2^{+H}}{k_1^{+H}} = \frac{k_2^{+D}}{k_1^{+D}} = \frac{2}{M^{1/2}K^{1/2}} \quad \text{and} \quad \frac{k_3^{+H}}{k_1^{+H}} = \frac{k_3^{+D}}{k_1^{+D}} = \frac{1}{M^{1/2}}$$

where $K = [HOD]^2/[H_2O][D_2O]$ and $L = \alpha^2_{H^+}[D_2O]/\alpha^2_{D^+}[H_2O] = M(k_3^{+D}/k_1^{+H})^2$. If we define the proton and deuteron activities by putting $k_1^{+H} = 1$, $k_3^{+D} = 1$, and we take $K = 3{\cdot}27$, $M = 15{\cdot}3$, we find that $\frac{3}{2}k_2^{+H} = 1{\cdot}05$ and $3k_3^{+H} = 1{\cdot}21$, which are in reasonable agreement with the constants determined experimentally by Orr and Butler, *viz.*, $\frac{3}{2}k_2^{+H} = 1{\cdot}05$, $3k_3^{+H} = 1{\cdot}10$.

The rate of a reaction in a mixed $H_2O$–$D_2O$ solution, which is determined by thermodynamic equilibrium, is given by

$$\kappa(n) = \alpha_{H^+}k_{H^+} + \alpha_{D^+}k_{D^+}$$

or

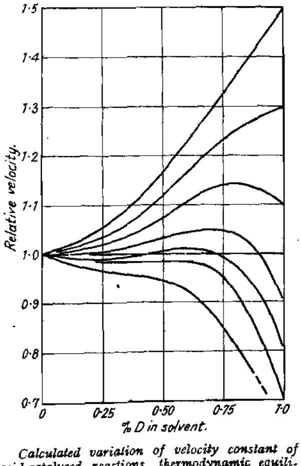
$$\kappa(n) = \Sigma H_3O^+ \,.\, f^+ \left\{\frac{k_1[H_2O]^{1/2} + k_2[D_2O]^{1/2}\sqrt{L}}{Q'(n)}\right\}$$

Values of $Q'(n)$, calculated from the theoretical constants given above, are as follows:

| | | | | | |
|---|---|---|---|---|---|
| $n$ ........................................ | 0·00 | 0·25 | 0·50 | 0·75 | 1·00 |
| $Q'(n)$ .................................. | 1·00 | 0·816 | 0·612 | 0·421 | 0·26 |

The curves calculated for various ratios of $\kappa(1)$ from these constants are shown in Fig. 1.

FIG. 1.




*Calculated variation of velocity constant of acid-catalysed reactions, thermodynamic equilibrium between the complex and the solution being assumed.*

Acid-catalysed reactions which have been found to follow the thermodynamic relati
are the decomposition of diazoacetic ester, hydrolysis of acetal, bromination of aceto

and (probably) the inversion of cane sugar; on the other hand, the mutarotation of α-glucose shows a large divergence. It is significant that so far as has been investigated all reactions which are faster in heavy water than in light water obey the thermodynamic relation, but no case has been found in which this holds for a slower reaction.

TABLE I.

Ethyl formate in 0·201N-H(D)Cl at 15·0° ± 0·05°.

| | | | | | | |
|---|---|---|---|---|---|---|
| $n$ | 0·00 | 0·27 | 0·72 | 0·82 | 0·96 | 1·00 |
| $n \times 10^3$ | 14·7 | 15·3 | 17·7 | 18·6 | 20·4 | (20·15)* |

$k_{D_3O^+}/k_{H_3O^+} = 1·37$

Methyl acetate in 1·317 N-H(D)Cl at 15·0° ± 0·05°.

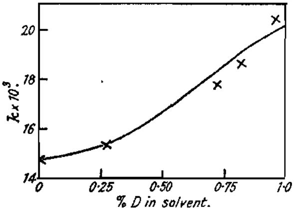
| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $n$ | 0·00 | 0·214 | 0·265 | 0·512 | 0·703 | 0·713 | 0·984 | 1·000 |
| $k \times 10^3$ | 3·87 | 4·08 | 4·32 | 4·47 | 5·03 | 5·17 | 6·12 | (6·20)* |

$k_{D_3O^+}/k_{H_3O^+} = 1·60$

* Extrapolated from theoretical curve.

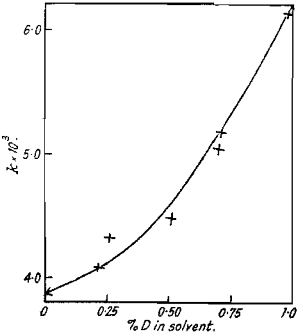
A case of some interest is the hydrolysis of simple esters, in which general catalysis by undissociated acids has been reported (Dawson, J., 1927, 2107, 2444). In this case there does not appear to be any possibility of a pre-equilibrium followed by general basic catalysis, as in the case of acetone, so that the shape of the curve should give conclusive evidence as to the existence of general acid catalysis. Measurements were made with ethyl formate and methyl acetate, and the results are shown in Table I, and Figs. 2 and 3 show the comparison with the calculated curves. The ethyl formate reaction was followed by observation of the refractive-index change in an interferometer. Considerable difficulty was experienced in obtaining stable final readings and the accuracy of the series is not great. For the methyl acetate reaction a direct micro-titration method was employed and the results are in close agreement with the thermodynamic relation. It must be concluded that the complex is in thermodynamic equilibrium with the medium, and general catalysis by acids is therefore improbable.

FIG. 2.




*Variation of velocity of hydrolysis of ethyl formate in* H(D)Cl *solutions with deuterium content of solution.*

FIG. 3.




*Variation of hydrolysis rate of methyl acetate in* H(D)Cl *solutions with deuterium content of solution.*

*Alkaline Catalysis of the Decomposition of Diacetone Alcohol.*—The variation with the deuterium content of the water of a reaction catalysed by alkalis has not previously been investigated. The variation of the activities of the hydroxyl and deuteroxyl ions with the composition of the water could be established by determinations of the dissociation constants

of a weak base, or alternatively by calculation from the constants given above, together with the dissociation constants of $H_2O$ and $D_2O$. Since those constants account successfully for the course of the hydrogen-ion catalysis, the latter method has been adopted. The relative concentrations of $OH^-$ and $OD^-$ are determined by the equation

$$2OD^- + H_2O = 2OH^- + D_2O.$$

Writing $N = [OH^-]^2[D_2O]/[OD^-]^2[H_2O]$

and $k_1^{-H} = [OH^-]a_{H^+}/[H_2O]$; $k_3^{-D} = [OD^-]a_{D^+}/[D_2O]$

we find that $N = \frac{1}{M}\left(\frac{k_1^{+H}k_1^{-H}}{k_3^{+D}k_3^{-D}}\right)^2 = \frac{1}{M}\left(\frac{K_{H_2O}}{K_{D_2O}}\right)^2$

where $K_{H_2O} = [H_3O^+][OH^-]$, $K_{D_2O} = [D_3O^+][OD^-]$.

Taking $K_{D_2O}/K_{H_2O}$ as 0·184 at 15° (Wynne-Jones, *Trans. Faraday Soc.*, 1936, **32**, 1397) and $M = 15{\cdot}3$, we have $N = 1{\cdot}93$.

Writing $\Sigma OH^- = [OH^-] + [OD^-]$ and $[OD^-]/[OH^-] = \sqrt{[D_2O]/N[H_2O]} = R(n)$,

we have $[OH^-] = \Sigma OH^-/[1 + R(n)]$

and $[OD^-] = \Sigma OH^-/[1 + 1/R(n)]$

Therefore, if the reaction rate is determined by the hydroxyl- and the deuteroxyl-ion activities, we have

$$\kappa(n) = k_1[OH^-] + k_2[OD^-]$$
$$= \Sigma OH^-[k_1 + k_2R(n)]/[1 + R(n)]$$

and the ratio of the rate in a given solution to that in similar circumstances in light water is

$$\zeta(n) = [1 + (k_2/k_1)R(n)]/[1 + R(n)]$$

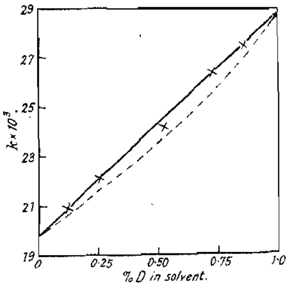
TABLE II.

Decomposition of diacetone alcohol in 0·1185N-NaOH(D) at 15° ± 0·05°.

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| $n$ .................. | 0·00 | 0·121 | 0·259 | 0·529 | 0·725 | 0·853 | 0·990 | 0·996 | 1·000 |
| $k \times 10^3$ ......... | 19·8 | 20·9 | 22·1 | 24·2 | 26·4 | 27·5 | 28·6 | 28·7 | (28·7) |

$k_{OD^-}/k_{OH^-} = 1{\cdot}45.$

FIG. 4.




*Alkaline decomposition of diacetone alcohol in* NaOH(D) *solutions.*
– – – *Calculated curve.*

Measurements were made of the rates of decomposition of diacetone alcohol in alkaline solutions of constant alkalinity; the results are given in Table II and the comparison with the calculated curve is shown in Fig. 4. The observed variation is practically linear, whereas

the calculated curve has a slight but definite sag. This certainly favours the view that the reaction does not proceed by way of an equilibrium complex, but the difference is too small to be conclusive.

In order to obtain more definite evidence, some " heavy " diacetone alcohol was prepared, containing 60·4% of deuterium, and its rate of decomposition in alkaline solutions in light and heavy water determined. In both cases it reacts appreciably more slowly than the " light " compound :

| | 0·1185N-NaOH in $H_2O$. | 0·1166N-NaOD in $D_2O$. |
|---|---|---|
| " Light " diacetone alcohol .................... | 19·8 | 29·2 |
| " Heavy " diacetone alcohol .................. | 15·8 (17·0) * | 26·6 |

* Original product prior to distillation.

The linearity of the rate with the deuterium content of the alcohol being assumed, the rate of decomposition of the heavy alcohol would be about 0·7 of that of the light compound. This is considerably greater than that observed in comparable cases, *e.g.*, in the neutralisation of heavy and light nitroethane, where the ratio is about 0·1, but the difference from unity seems too great to be ascribed merely to the effect of the additional mass of the deuterium atoms in the molecule.

It is therefore concluded that the rate-determining step is a proton (or deuteron) transfer from the compound to the hydroxyl (deuteroxyl) ion, and the mechanism given in the summary (p. 958) is indicated. The proton would most naturally be lost from one of the terminal methyl groups adjacent to the hydroxylic oxygen. This half of the molecule is thus converted into enolic acetone, and the molecule would then split into an enolic acetone molecule and the corresponding ion. This accounts for all the main features of the reaction : (1) The " heavy " alcohol reacts more slowly because the transfer of $D^+$ from the compound to $OH^-$ or $OD^-$ is slower than the corresponding transfer of $H^+$. (2) The " light " alcohol reacts more quickly in $D_2O$ than in $H_2O$, because the rate of transfer of a proton to the deuteroxyl ion is more rapid than to a hydroxyl ion; *e.g.*, Wynne-Jones (*J. Chem. Physics*, 1934, **2**, 281) found that the rates of neutralisation of nitroethane in alkaline solutions in light and in heavy water were in the ratio 39 : 60. (3) The reaction is not catalysed by acids. The enolisation of the terminal acetone cannot be effected by acid catalysis because the oxygen is already in the hydroxylic form.

## EXPERIMENTAL.

The diacetone alcohol reaction gives rise to a marked change of refractive index and its progress could easily be followed by the interferometric method previously described. The temperature control in the interferometer was considerably improved by filling all the space inside the water jacket not occupied by the cell or required for the beams of light by massive blocks of metal. The concentration of the alcohol was kept constant throughout the series of solutions, which were made by addiug 0·025 c.c. of alcohol to 1 c.c. of solution.

The heavy diacetone alcohol was prepared as follows. Acetone was mixed with an equal volume of " heavy " water (actually the residues from kinetic experiments and containing acetone and alkali) and heated in a sealed vessel at abont 70° for 2 days. The acetone was then recovered by fractional distillation and treated with a further quantity of heavy water in the same way. The resulting " heavy " acetone was condensed by refluxing in a small Soxhlet extractor, the condensate running through a thimble of heavy baryta (Conant and Tuttle, " Organic Syntheses," Vol. I, 45). After 3 days the product was fractionated and a good yield of the alcohol obtained.

We thank Messrs. Imperial Chemical Industries Ltd. and the Earl of Moray Endowment for grants, and we are indebted to Dr. C. L. Wilson, of University College, London, for making the analysis of the heavy diacetone alcohol.

KING'S BUILDINGS, WEST MAINS ROAD, EDINBURGH. [*Received, April 30th*, 1938.]

# 180. *The Reaction between Amines and Unsaturated Compounds containing Halogen attached to one of the Ethylenic Carbon Atoms. Part II. The Preparation and Constitution of some New Diamines.*

By John C. Roberts.

Reactions similar to that between ethyl α-chlorocrotonate and dimethylamine (Part I, J., 1936, 1169), which involves addition at the point of unsaturation and replacement of the halogen by the dimethylamino-group, have been investigated. The most successful results have been obtained with dimethylamine and piperidine.

Piperidine and dimethylamine, in alcoholic solution, react readily with ethyl α-chlorocrotonate or ethyl α-bromocinnamate to yield substituted diamino-esters; *e.g.*, $CHMe{:}CCl{\cdot}CO_2Et + 3NHMe_2 = NMe_2{\cdot}CHMe{\cdot}CH(NMe_2){\cdot}CO_2Et + NHMe_2,HCl$. With 3 mols. of the base the reaction proceeds almost to completion, without application of heat, within 20 hours—sometimes within a very much shorter time. Side reactions do not occur to any appreciable extent and good yields are obtained. Ammonia and methylamine give much less definite results.

In all the reactions the rate of production of ionisable halogen was followed approximately, and as far as conditions would permit, by acidification and titration of aliquot portions of the mixture. The bases were used in approximately equimolecular concentrations. Dimethylamine and, to a less extent, piperidine produced ionisable halogen most readily. Methylamine and ammonia displaced a considerable amount (70—80%) of the halogen, but diamino-esters were not isolated; more complicated reactions apparently took place.

The αβ-structure is assigned to the new diamines, although the investigations of Dufraisse and Moureu (*Bull. Soc. chim.*, 1927, **41**, 457, 850) on the reactions between amines and α-halogenated αβ-unsaturated ketones do not exclude the αα-structure, and the hydrolysis of *ethyl bis(dimethylamino)-β-phenylpropionate* by dilute sulphuric acid yields a snbstance which appears to be a mixture of phenylglycidic and phenylpyruvic acids, the former indicating an αβ-structure and the latter an αα-structure. Phenylglycidic acid, however, is partly converted into phenylpyruvic acid by heating with mineral acids (Erlenmeyer, *Ber.*, 1900, **33**, 3001: cf. also the change of phenylethylene oxide into phenylacetaldehyde; Zinke, *Ber.*, 1878, **11**, 1402). There is therefore no evidence against phenylglycidic or phenylglyceric acid being the first product of hydrolysis.

Theoretical considerations favour the αβ-structure for the diamines. Halogen attached to an ethylenic carbon atom is firmly held. This would indicate that addition of the amine to the unsaturated compound takes place before elimination of halogen occurs. The unsaturated halogenated compounds referred to above all contain a conjugated unsaturated system, are capable of mesomeric change, and can therefore exist as resonance hybrids of the two forms

$$R{\cdot}CH{:}C(Hal.){\cdot}\overset{\overset{O}{\|}}{C}{\cdot}R_1 \text{ and } R{\cdot}\overset{\oplus}{C}H{\cdot}C(Hal.){:}\overset{\overset{O^{\ominus}}{|}}{C}{\cdot}R_1$$
$$(R = Me \text{ or } Ph;\ R_1 = OEt \text{ or } Ph)$$

Amines are well-recognised nucleophilic reagents (cf. Chattaway, J., 1936, 355), indicating that attachment of the amino-group will take place on the β-carbon atom.

## Experimental.

*Reaction between Ethyl α-Chlorocrotonate and Piperidine.*—1·08 G. of the ester (J., 1936, 1170; this vol., p. 779) were mixed with 2·15 c.c. of piperidine (3 mols.) in 4·7 c.c. of absolute alcohol; some heat was evolved. After ½ hour, 0·6 c.c. of the mixture was added to 10 c.c. of dilute nitric acid; titration with 0·1N-silver nitrate indicated that about 63% of the chlorine had been removed from the ester. After 45 minutes, long needle-shaped crystals separated, preventing the further abstraction of aliquot portions.

*Ethyl αβ-Dipiperidinobutyrate.*—A mixture of 6·17 g. of ethyl α-chlorocrotonate, 12·3 c.c.

of piperidine (3 mols.), and 28·3 c.c. of absolute alcohol was after 2 hours neutralised with concentrated hydrochloric acid (about 4 c.c.), and alcohol (18 c.c.) distilled off on the water-bath The residual crystals were cooled in ice and treated with 40 c.c. of ice-cold water. The cloudy reddish-brown solution was acidified with concentrated hydrochloric acid (4 c.c.), shaken with ether (15 + 15 c.c.), and basified with ice-cold 33% sodium hydroxide solution. The yellow oil obtained was extracted with ether (20 + 15 + 10 c.c.), washed with water (10 + 10 c.c.), and dried (sodium sulphate), the solvent evaporated, and the residue distilled in a vacuum, yielding 7·4 g. of *ethyl* αβ-*dipiperidinobutyrate* as a pale yellow, very viscous oil of pronounced basic and rather unpleasant odour, b. p. 181—183°/14 mm., practically insoluble in water (Found C, 68·1; H, 10·5; N, 9·7. $C_{16}H_{30}O_2N_2$ requires C, 68·1; H, 10·6; N, 9·9%).

*Reaction between Ethyl α-Bromocinnamate and Dimethylamine.*—2·28 G. of the ester were mixed with 3·84 g. of a 33% solution of dimethylamine (3 mols.) in absolute alcohol. After 10 minutes considerable heat was evolved and the mixture was cooled in running water. After 1½ hours, an excess of dilute nitric acid (30 c.c.) was added, and the volume made up to 100 c.c. titration of 10 c.c. with 0·1N-silver nitrate indicated that about 95% of the bromine had been removed from the ester.

*Ethyl* αβ-*Bis(dimethylamino)*-β-*phenylpropionate.*—9·5 G. of ethyl α-bromocinnamate were mixed with 15·2 g. of a solution of the base (3 mols.), with subsequent cooling as described above After 15 minutes crystals of dimethylamine hydrobromide separated and after 1½ hours the product was isolated in the way described above in the case of ethyl αβ-dipiperidinobutyrate *Ethyl* αβ-*bis(dimethylamino)*-β-*phenylpropionate* (6 g.) was obtained as a colourless viscous oil of rather unpleasant odour, b. p. 154—155°/8 mm., practically insoluble in water (Found: C 68·0; H, 8·9; N, 10·5. $C_{15}H_{24}O_2N_2$ requires C, 68·2; H, 9·1; N, 10·6%); after several months keeping in a stoppered bottle it formed prisms, m. p. 37—38°. The *platinichloride* crystallised in deep orange-coloured pyramids, m. p. 185° (decomp.) (Found: Pt, 28·5. $C_{15}H_{24}O_2N_2,H_2PtCl_6$ requires Pt, 29·0%). The picrate separated from acetone in small, yellow, irregular prisms m. p. 148—149°; from alcoholic solutions two distinct crystalline compounds separated, which were not investigated. The *dihydrochloride* was prepared by means of ethereal hydrogen chloride. The white crystalline precipitate obtained, when dissolved in absolute alcohol and reprecipitated by ether, separated as a glue. This was placed in a vacuum over concentrated sulphuric acid, powdered, and again dried in the same manner (Found: Cl, 20·3. $C_{15}H_{24}O_2N_2,2HCl$ requires Cl, 21·1%). Hydrogen chloride was lost on drying in a vacuum. Other methods of drying were unsuccessful.

*Reaction between Ethyl α-Bromocinnamate and Piperidine.*—1·94 G. of the ester were mixed with 2·3 c.c. of piperidine (3 mols.) dissolved in 5·0 c.c. of absolute alcohol. By titration of aliquot portions it was found that about 46% of the bromine had been replaced after 1 hour and about 69% after 2 hours; crystals then separated.

*Ethyl* αβ-*Dipiperidino*-β-*phenylpropionate.*—6·4 G. of ethyl α-bromocinnamate were treated with 7·4 c.c. of piperidine (3 mols.) dissolved in 17 c.c. of absolute alcohol; the temperature rose to 31° after 1 hour. After 12 hours, the almost solid, crystalline mass was shaken with 20 c.c. of water and 6 c.c. of 33% sodium hydroxide solution and the cream-coloured precipitate which separated was washed successively with water, 45% alcohol (30 c.c.), and water, dried (yield, 8·4 g.), recrystallised from a small quantity of boiling alcohol (95%) in a continuous extraction apparatus, and dried in a vacuum over concentrated sulphuric acid. *Ethyl* αβ-*dipiperidino*-β-*phenylpropionate* was obtained as a pale cream-coloured powder—very small, colourless crystals when seen under the microscope—m. p. 74—75°, practically insoluble in water and rather sparingly soluble in alcohol (Found: C, 73·5; H, 9·1; N, 8·2. $C_{21}H_{32}O_2N_2$ requires C, 73·2; H, 9·3; N, 8·1%). A dihydrochloride, which readily lost hydrogen chloride, and a picrate (yellow prisms, m. p. 122—123°, from alcohol) were prepared, but a pure platinichloride could not be obtained; on attempted recrystallisation from water a strong odour of benzaldehyde was observed.

*Degradation of Ethyl* αβ-*Bis(dimethylamino)*-β-*phenylpropionate.*—(i) *With alkali.* 0·246 G. of the ester was refluxed for 6 hours with 6 g. of potassium hydroxide in 30 c.c. of water. Air bubbling through the boiling solution and for 2 hours during cooling was drawn through the condenser into two absorption flasks containing 25 c.c. and 10 c.c. of 0·1N-sulphuric acid. The alkaline gases evolved neutralised 7·1 c.c., corresponding to about a 76% liberation of one of the dimethylamino-groups as dimethylamine. By concentration of the neutralised acid, decomposition by boiling with excess of sodium hydroxide solution, and passage of the gas evolved through an alcoholic solution of picrolonic acid, a light yellow, crystalline precipitate was obtained. After recrystallisation from alcohol this was identified as dimethylamine picrolonate

—it lost its crystalline shape and colour at 222° and decomposed vigorously at 232°, behaving identically with an authentic sample. After another 3 hours' refluxing, with fresh standard acid in the absorption flasks, a theoretical titre was obtained. The residue in the reaction flask had a strong odour of benzaldehyde.

(ii) *With dilute sulphuric acid.* (a) 0·95 G. of the ester was refluxed for 20 minutes with 10 c.c. of 15% sulphuric acid; after a few minutes, oily drops were observed in the condensate. 10 C.c. of water were added, and 10 c.c. distilled. The distillate gave with 100 c.c. of a solution of 2 : 4-dinitrophenylhydrazine (0·33% in 2N-hydrochloric acid) a precipitate which, recrystallised from benzene–alcohol and examined under the microscope, was seen to consist of two crystalline substances. On cooling, the liquid in the distillation flask gave a crystalline precipitate. This was extracted with ether, the ether evaporated, and the product recrystallised from 5% alcohol; it melted over a range of 20°. An attempt to purify it by precipitation with acid from warm sodium carbonate solution was not successful, an emulsion being produced which had an odour resembling that of hyacinths. Phenylglyceric or phenylglycidic acid was therefore suspected.

(b) In another similar experiment, the ethereal extract was washed with water, the ether evaporated, and the residue recrystallised from warm ether–benzene. The product was dried at 100° for 20 minutes and then over calcium chloride in a desiccator. Lustrous leaflets (0·23 g.) were obtained which under the microscope appeared as long prisms. The m. p. was indefinite and varied according to the rate of heating; a meniscus formed at 143° on very slow heating (Found: C, 65·8; H, 5·0. Calc. for phenylglycidic or phenylpyruvic acid, $C_9H_8O_3$: C, 65·9; H, 4·9%). An ethereal solution of the product gave the characteristic colour reaction for phenylpyruvic acid with dilute aqueous ferric chloride. When the product was warmed with sodium carbonate solution, an odour of phenylacetaldehyde was evolved. It was therefore concluded that the product was a mixture of phenylpyruvic and phenylglycidic acids.

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UNIVERSITY COLLEGE, NOTTINGHAM. [*Received, April 27th,* 1938.]

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# NOTES

*The Interaction of* l-β-*Octyl Nitrite and* dl-β-*Butanol.* By J. KENYON and D. P. YOUNG.

It is well known that the alkyl group of a nitrous ester is exchanged with very great ease and rapidity for that of an alcohol in which it is dissolved, and the suggestion has been made (*vide* "The Organic Chemistry of Nitrogen," Sidgwick, 1937) that the ready exchange may be due to complex formation according to the equation:

$$\mathrm{O{:}N{\cdot}OR} + \mathrm{R'OH} \rightleftharpoons \mathrm{O{\leftarrow}N(OR)(OR')(H)} \rightleftharpoons \mathrm{O{:}N{\cdot}OR'} + \mathrm{R{\cdot}OH}.$$

In an attempt to obtain evidence bearing on this suggestion, *l*-β-octyl nitrite was gently heated with two molecular proportions of *dl*-β-butanol, as it was thought possible that the optically active ester might combine preferentially with the *d*- or the *l*-form of the alcohol, in which case both the β-butyl nitrite produced and the uncombined butanol would be optically active. Although the reaction proceeded smoothly and completely, both the resulting β-butyl nitrite and the recovered β-butanol were devoid of optical activity; the other product of the reaction, *l*-β-octanol, was isolated in a state of optical purity.

The interesting hypothesis mentioned above remains, therefore, still unproven.

*l*-β-Octyl nitrite was prepared by passing nitrosyl chloride into a well-cooled solution of *l*-β-octanol in four times its weight of pyridine (cf. Pickard and Hunter, J., 1923, **123**, 441). Next day the mixture was shaken with water, and the ester extracted with ether, washed with dilute acid, dried, and distilled (yield, 80%). It was a pale yellow, mobile liquid of pleasant odour, b. p. 63—65°/15 mm., $n_D^{18.5°}$ 1·4202, $d_{4°}^{18°}$ 0·861, $\alpha_{5461}^{18°}$ − 1·13° (*l*, 0·25), whence $[\alpha]_{5461}$ − 5·28° (Shriner and Young, *J. Amer. Chem. Soc.*, 1930, **52**, 3332, who obtained this compound as a by-product from the interaction of β-octyl bromide and silver nitrite, give $n_D^{20°}$ 1·4218, $d_{20°}^{20°}$ 0·857, $[\alpha]_D$ − 6·85° in alcoholic solution).

When a mixture of *l*-β-octyl nitrite (7·9 g.) and *dl*-β-butanol (7·4 g.; 2 mols.) was slowly distilled through a short fractionating column, *dl*-β-butyl nitrite, b. p. 70—75°, readily came over, followed by unchanged *dl*-β-butanol, b. p. 98—105°. The residual *l*-β-octanol, b. p. 83—85°/20 mm., was of unchanged rotatory power.

The experiment was repeated, the mixture of octyl nitrite and butanol being kept at room temperature for 3 days before distillation: the result, however, was the same.—Battersea Polytechnic, London, S.W. 11. [*Received, April 28th*, 1938.]

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*Manganese Perchlorate and Per-rhenate.* By J. Gerald F. Druce.

Manganese perchlorate was prepared by Serullas (*Ann. Chim. Phys.*, 1831, **46**, 297) by the interaction of barium perchlorate and manganese sulphate. It has also been prepared by the action of perchloric acid upon manganese chloride (private communication from Prof. G. Frederick Smith of Urbana, Ill.). A more convenient method was to dissolve manganese carbonate in perchloric acid, filter off any undissolved carbonate, and allow the filtrate to concentrate in a vacuum over anhydrous magnesium perchlorate. Pale pink, deliquescent needle prisms separated [Found: $ClO_4'$, 53·8; Cl, 18·9. $Mn(ClO_4)_2,6H_2O$ requires $ClO_4'$, 55·0; Cl, 19·4%]. The crystals melted at 155°, and began to decompose at 165° with evolution of water vapour, oxygen (glowing splint rekindled), and oxides of chlorine (colourless gas which bleached litmus). Decomposition was rapid at 230°, and the black residue, after complete decomposition, was found to be manganese dioxide, free from chlorine. Anhydrous manganese perchlorate could not be isolated in a pure state.

*Manganese per-rhenate* was obtained in deliquescent, pink, prismatic needle crystals by dissolving manganese carbonate in per-rhenic acid and concentrating the solution in a vacuum desiccator over magnesium perchlorate. The crystals were dried on porous plate in a desiccator [Found: $H_2O$, 9·0. $Mn(ReO_4)_2,3H_2O$ requires $H_2O$, 8·9%]. The anhydrous salt [Found: Re, as nitron per-rhenate, 66·5; Mn, as $Mn_3O_4$, 9·63. $Mn(ReO_4)_2$ requires Re, 67·5; Mn, 10·0%] was pink and readily absorbed water to form a solution of the per-rhenate. The anhydrous salt did not melt below 300°. At somewhat higher temperatures rhenium heptoxide volatilised and a dark residue, finally $Mn_3O_4$, remained.

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